A STUDY ON GLUCOSE TOLERANCE TEST IN YOUNG SPUTUM POSITIVE TUBERCULOSIS PATIENTS

Dissertation submitted

in partial fulfillment for the Degree of

DOCTOR OF MEDICINE

BRANCH I - M.D., (General Medicine)

MARCH 2007

DEPARTMENT OF MEDICINE

MADURAI MEDICAL COLLEGE

THE TAMILNADU DR.M.G.R. MEDICAL UNIVERSITY

CHENNAI – TAMILNADU

CERTIFICATE

This is to certify that this dissertation entitled **"A STUDY ON GLUCOSE TOLERANCE TEST IN YOUNG SPUTUM POSITIVE TUBERCULOSIS PATIENTS"** submitted by **Dr.USHANAGADEVI C.S.** to The Tamil Nadu Dr.M.G.R. Medical University, Chennai is in partial fulfillment of the requirement for the award of M.D. degree Branch I (General Medicine) and is a bonafide research work carried out by her under direct supervision and guidance.

Dr. Moses .K. Daniel M.D.,
Additional Professor,
Department of Medicine,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

Dr. Nalini Ganesh M.D.,
Professor and Head,
Department of Medicine,
Govt. Rajaji Hospital,
Madurai Medical College,
Madurai.

DECLARATION

I **Dr. USHANAGADEVI C.S** declare that I carried out this work on **"A STUDY ON GLUCOSE TOLERANCE TEST IN YOUNG SPUTUM POSITIVE TUBERCULOSIS PATIENTS"** at Department of General Medicine, Government Rajaji Hospital during the period of August 2005 – July 2006. I also declare that this bonafide work or a part of this work was not submitted by me or any other for any award, degree, diploma to any university, board either in India or abroad.

This is submitted to the Tamilnadu Dr.M.G.R. Medical University, Chennai in partial fulfillment of the rules and regulation for the M.D. Degree examination in General Medicine.

Madurai Medical College, **Dr. USHANAGADEVI C.S.**

Madurai.

ACKNOWLEDGEMENT

My sincere thanks to The Dean **Dr. S.M.Sivakumar M.S.,** for permitting me to use the facilities of Madurai Medical College and Government Rajaji Hospital to conduct this study.

My Professor and Head of the Department of Medicine Prof. **Dr. Nalini Ganesh, M.D.,** who has always guided me, by example and valuable words of advice throughout the conduct of the study and also during my post graduate course. My sincere thanks to her.

I will ever remain in gratitude to my Chief **Dr.Moses K. Daniel, M.D.,** Addl. Professor of Medicine, not only for guiding me throughout this study, but also for being my mentor and source of inspiration during my postgraduate training.

My heartfelt thanks to my beloved teachers, **Dr. A. Ayyappan M.D., Dr. P. Selvaraj M.D., Dr.M.Kamaraj M.D., Dr.D.D.Venkatraman M.D.,** and **Dr. M.Muthiah M.D.,** I owe them a lot.

Dr. David Pradeep Kumar M.D., Dr.K.Senthil M.D., Dr.V.Ramakrishnan M.D., Assistant Professors of Medicine have always been helpful to me to complete this study. I sincerely thank them.

My sincere thanks to **Dr.Arthur Joseph Asirvatham M.D., D. Diab. Dr. R.Sundaram M.D., Dept. of Diabetology, Dr.C.Ramesh M.D., DTCD**

Dr. S.C. Vivekananthan M.D. (Gen) DTCD, Dr. S. Prabhakaran MBBS DA., for helping me to carryout the necessary investigations and guiding me.

I also thank Assistant Professor **Dr. S.Somasundaram M.D.,** for his valuable support and guidance.

My former Professor and Head of the Department of Medicine, **Prof. Dr. P.Thirumalaikolundu Subramanian M.D.,** has always guided me by example and valuable words of advice. My sincere thanks to him.

Support given by my senior and junior colleagues is duly acknowledged here. I express my gratitude by thanking them.

I thank my family and friends who have contributed a lot to my life and made it wonderful.

I duly acknowledge the co-operation and support provided by the patients without whom the work couldn't have been completed. I pray to the Almighty for their well being.

Above all I thank the Lord Almighty for his kindness and benevolence.

ABBREVIATIONS

TB	-	Tuberculosis
DM	-	Diabetes Mellitus
WHO	-	World Health Organization
RNTCP	-	Revised National Tuberculosis Control Programme
OGTT	-	Oral Glucose Tolerance Test
ADA	-	American Diabetology Association
N	-	Normal
IFG	-	Impaired Fasting Glucose
IGT	-	Impaired Glucose Tolerance
AFB	-	Acid Fast Bacillus
ATT	-	Anti Tuberculosis Treatment
HIV	-	Human Immuno Deficiency Virus
CVA	-	Cerebro Vascular Accident
GRH	-	Government Rajaji Hospital
TNF	-	Tumour Necrosis Factor
IL	-	Interleukin
HbA_1c	-	Glycosylated Haemoglobin

INTRODUCTION

Tuberculosis and Diabetes mellitus are among the top rated diseases in the Indian population, with significant effects on morbidity and mortality of the community, and producing a great impact on the economical aspects of the society.

To find out the correlation and coexistence of both the diseases are very important as they influence the clinical course and therapeutics of each other. It has been postulated that in the context of economic development, a country's health issues will evolve from infectious to noninfectious diseases. In reality, this transition more commonly simply adds chronic conditions to a public health system already burdened by infectious disease. In many settings, this process will result in the convergence of two epidemics: Diabetes and Tuberculosis[1].

There is now recognition of an explosive epidemic called Diabetes in India and in this pandemic invasion of Diabetes, the diagnosed cases forms just a tip of the iceberg. WHO has projected that maximum increase in diabetes would occur in India[2].

Tuberculosis and diabetes frequently coexist together and there is a growing amount of evidence of one disease fueling the other.

Symptoms of one disease often mimic those of the other. Loss of weight, loss of appetite and lassitude are common to both diseases. The association is more common among those above 40 yrs of age.

Diabetes appears to have an induction and aggravating effect on tuberculosis. Tuberculosis was found to be more pronounced in diabetes, had more pronounced radiological signs, treatment failures and deaths were also frequent .

Diabetes mellitus has been reported to modify the presenting features of pulmonary tuberculosis but their conjoint presence does not alter the symptomatology, bacteriology and tuberculin reaction. Some studies have even indicated that MDR.TB is more common in diabetes than in non diabetic population.

Tuberculous patients who develop diabetes have greater clinical severity at the onset, a greater degree of lung involvement and residual changes.

The implications of these issues throw up numerous problems of basic, applied and operational nature and the possibility of drug interactions between

the two therapeutic groups contribute a lot to the difficulty in successfully treating this brewing double trouble.

Since simple tests like sputum analysis and blood sugar estimation will make a definitive diagnosis of pulmonary tuberculosis and diabetes mellitus respectively, the knowledge of the degree of coexistence of these diseases should make the treating doctor to search for the other disease when one is diagnosed.

The diagnosis of coexisting diabetes in TB patients will also help in early treatment of the same and retardation of various complications of diabetes like renal impairment, CAD, stroke etc. which are important factors adversely affecting prognosis of patients with tuberculosis sequelae if they do occur.

Currently in India approximately 20 million people suffer from diabetes but less than 12% receive pharmacological treatment. It has been projected that by the year 2025, there would be 57.2 million diabetics in India[2]. Diabetics are high risk group for tuberculosis, especially insulin dependent patients whose risk is about 38 times higher than the general population.

India is also the home to the largest number of tuberculosis patients in any one country. And there is a growing amount of evidence of one disease fueling the other. The interest in diabetes and tuberculosis is mounting rapidly

and it promises to be an exciting time for researchers and clinicians involved in the study of dual diseases. There are numerous issues of basic, applied and operational research waiting for solutions.

It is a wake-up call for all clinicians and researchers to gear-up to meet the challenge of the brewing double trouble.

Many studies have explored the association between diabetes and tuberculosis. In developed countries, studies dating to the first half of the past century demonstrated considerable increase in the frequency of tuberculosis among patients with diabetes although the proportion with co morbidity has ranged widely from 1.0[3] to 9.3%[4]. Other studies have shown a higher frequency of diabetes among individuals with tuberculosis[5,6]. Similar results were found in the few studies that have addressed this association in developing countries.

Hence an attempt has been made through this study to identify the prevalence of IGT and Diabetes Mellitus among young sputum positive pulmonary tuberculosis patients in Madurai and to find out the significance of the same.

REVIEW OF LITERATURE

Historical aspects of diabetes

Early evidence of description of the symptoms of diabetes in Ebers papyrus – 1550B.C [Shafir E 1999][8].

Early description of polyuria by Imhotep 3000 B.C. [Shafir E – 1999][8]

Aratecus coined the term diabetes in AD 150.

Susrutha in India described the diabetic syndrome as characterized by honeyed urine [Schadewaldt – H] 1987[9].

1914-1919- methods for analysis to measure glucose as major reducing substance in serum and urine were devised. [Benedict S.R – 1918][10]

1869 – Paul Langerhans identified islets of Langerhans [Lagusse E. 1984][11]

1910 – Jean de Meyer coined the term insulin – for pancreatic secretion which was lacking in diabetes.[12]

1922 – Insulin was discovered by the team – Fredrick Banting, John Macleod, Charles Best and J.B Collip.[13]

1923 – Nobel prize in Medicine for insulin.[14]

Definition of diabetes mellitus[7]

It is characterized by hyperglycaemia with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, action and or both.

Epidemiology of Diabetes

Global – The global prevalence of diabetes is estimated to increase from 4% in1995 to 5.4% by the year 2025.[15] The WHO has projected that major burden will occur in developing countries. There will be a 42% increase from 51 to 72 million in the developed countries and 170% increase from 84 to 228 million in developing countries. The countries with the largest number of diabetic people are, and will be in the year 2025, India, China and United states.[15]

Indian scenario – A national survey of diabetes conducted in six major cities in India in the year 2000 showed that prevalence of diabetes in Indian adults was 12.1%. The prevalence of IGT was also high 14%[16]. A younger age of onset is also noted in Indians in several studies.[16,17]

Urban–rural difference-An urban–rural difference in the prevalence rate was found indicating that the environmental factors related to urbanization had a significant role in increasing the prevalence of diabetes[18]. The prevalence

of diabetes in urbanizing rural population was found to be midway between the rural and urban populations[19].

History of Tuberculosis

It's a disease of great antiquity. Tuberculosis lesions have been found in the vertebrae of Neolithic man in Europe and on Egyptian mummies dating possibly from as early as 3700 BC.[20]

Robert Koch – first described the tuberculosis bacillus now known as mycobacterium tuberculosis in 1882.[21]

M. tuberculosis, M. bovis and M. africanum are recognised as tubercle bacilli. M. tuberculosis is an obligate parasite that is infectious to human other primates and many other mammals.

Epidemiology of tuberculosis

Global - In 1993, the World Health Organization declared Tuberculosis as a global emergency because of the scale of the epidemic and the urgent need to improve global tuberculosis control.

According to tuberculosis case notification and rates by WHO in 2005, three regions dominate the world wise distribution and notification i.e., South

East region 36% African region 24% and Western pacific region 20% (Maher and Raviglione 2005).[22]

Table 1: Tuberculosis case notification and rates by WHO region in 2005

WHO region	No. of cases notified	Proportion of global total (%)
South East Asia	1,487,985	36
Africa	992,054	24
Western Pacific	806,112	20
America	233,648	9
Eastern Mediterranean	188,458	6
Europe	373,497	5

Source: Clinics in Chest medicine 2005

In 2005, there was an estimated 8.8 million new cases of tuberculosis world wide, with an incidence rate of 141 per 1,00,000 population.

Indian scenario (National Tuberculosis Institute)

Prevalence rate of tuberculosis infection in Indian population – 30%

Annual incidence of rate of infection – 1%

Prevalence of disease 337 to 406 / 1,00,000 population.

Annual incidence rate of disease – 70 to 132 /100,000 population.

TB and DM : A Brewing double trouble

As far back as 600 AD, the association of the two diseases (TB and DM) was noted by Susrutha[23]. Avicenna was reported to have noted this association more than thousand years ago[24].

The relationship between Diabetes Mellitus and tuberculosis dates back to Roman times. Autopsies in the 18th and 19th centuries were supportive of this association, although the tubercle bacillus was not discovered until 1882.

Presently, an epidemic of diabetes is occurring both in developed and developing nations. With the recognition of this explosive increase in the number of people diagnosed with diabetes mellitus all over the world, a whole new field of issues related to interaction between diabetes and pulmonary tuberculosis has been thrown open[25].

The global figure of people with diabetes is projected to rise from the current estimate of 150 million to 220 million in 2010 and 300 million in 2025[26]. Most cases will be of Type-2 diabetes, which is characterized by insulin resistance and / or abnormal insulin secretion.

The diabetic epidemic, although apparent across the world, has been most pronounced in non-European population, as evidenced by studies in the

native American and Canadian communities, Pacific and Indian Ocean island populations, groups in Indian and Australian aboriginal communities.[26]

The potential for increase in the number of cases of diabetes is greatest in Asia. Type –2 diabetes in children, teenagers, and adolescents is a serious new aspect to the epidemic and is an emerging public problem of significant proportions.

Based on compilation of studies from different parts of the globe, the World Health Organization has projected that the maximum increase in diabetes would occur in India.[26] Considering the large population and the high prevalence of diabetes, the burden of diabetes could be enormous. With an estimated 23 million today and the numbers set to increase to 57 million by 2025, the increasing prevalence of diabetes reflects the sedentary life-style, excessive energy intake, reduced physical activity and obesity[26].

Studies conducted in India in the last decade have highlighted that, not only is the prevalence of Type-2 diabetes high, but also that it is increasing rapidly in the urban population. Of particular interest are the results of three diabetic surveys conducted in Chennai in 1989, 1995 and 2000. They show a rising trend for diabetes mellitus and glucose intolerance. The period between 1989 and 1995 show a 40% rise in the prevalence[27]. A nation-wide study

conducted in six major cities in India in the year 2000 showed that the prevalence of diabetes in urban adults aged more than 20 years was 12.1%. Onset of diabetes occurs at younger age in Indians. The prevalence of impaired glucose tolerance test, which is a fore-runner of diabetes, is also increasing especially among the younger populations[27].

It is generally accepted that pulmonary tuberculosis is more prevalent among diabetics than in non-diabetics. This increase in tuberculosis morbidity among diabetics has strongly been substantiated by studies of the incidence of this combination. These statistical analysis have been made either on diabetic patients, material being taken from the case histories, in the medical wards and special diabetes hospitals and in the diabetic out patient clinics, or as autopsy findings and tuberculosis notifications, or on the prevalence being estimated by the finding of diabetics among the tuberculosis patients, admitted or on the out patient register of sanatoria or chest clinic specially dealing with tuberculosis patients. The prevalence of diabetes mellitus in tuberculosis population should be compared with that of general population to find whether tuberculosis patients suffer more from diabetes or vice-versa. Such a study in fact should be a synchronous survey of the definite population groups for both tuberculosis and diabetes.

If the percentage of tuberculosis patients among diabetics exceeds that of tuberculosis patients in the average population, there will also be relatively more cases of diabetes among patients with tuberculosis than in the total population and vice-versa. Unfortunately such a study is not available[28].

It is also true that the basic variations are involved firstly in the source of diabetes or tuberculosis patients, whether out patient clinic, private practitioner, ambulatory or hospitalized patients, or autopsy, secondly in age, race, sex, weight, duration of illness, age of onset of diabetes; thirdly in geographic area, in diagnostic criteria used, and in inadequacy in sample size.

Studies conducted after the introduction of the glucose tolerance test in 1950s, have shown high prevalence of impaired glucose tolerance test in patients with tuberculosis with rates ranging from 2 to 41%[29]. The use of different criteria for diagnosis of diabetes mellitus makes comparisons between the results of the studies almost impossible.

There have been reports of high prevalence rates of diabetes in cases of pulmonary tuberculosis (4-20%) and rates are higher for impaired glucose tolerance test (16-29%). After anti-tuberculosis therapy, 50% of them had normalization of glucose intolerance. Some investigators have reported an association between severity of tuberculosis and abnormal glucose tolerance.

However, no association has been found with age, family history of tuberculosis, ethnicity or duration of treatment.[30]

Time relationship between TB and DM

It is universally accepted that among the diabetics who suffer from tuberculous disease, it is the diabetes, which antedates the onset of tuberculosis. In an earlier analysis Mark and associates[31] have found in a series of 349 patients, diabetes preceded tuberculosis in 60 percent and Reaud[32] reported in a series studied in early fifties that more than 50 percent of the patients had suffered from diabetes for more than 5 years. Ferrara[33] reported 69 percent of diabetic tuberculosis patients of his series of 68 patients in whom diabetes antedated the tuberculosis.

Boucots[43] postulation that increasing prevalence of tuberculosis should be observed with increasing duration of diabetes could be held valuable only with regard to younger diabetics. The tuberculosis prevalence for those below 40 years was 5 percent with diabetes of less than 10 years duration, compared to 17 percent those with diabetes of more than 10 years duration. But for those patients over the age of 40, the prevalence of tuberculosis was only 8 percent regardless of the duration of diabetes. Though the series is small, the finding that 56.6 percent of cases of tuberculosis had only a history of diabetes of less than one year, and 31.1 percent had a diabetic history of 1 to 5 years duration

compared to 10.3 percent with diabetic history varying from 6 to 15 years in the series of Jha[35] et al (1980) who also points to the fact that the duration as such is not important. Similar were the conclusions of Deshmukh et al[40] (1962) and Patel[36]et al (1977).

The point, which has to be emphasized is that, a known diabetic who has no reaction to tuberculin can have a check up at longer intervals compared to the 'reactors' who should be subjected to more strict surveillance and tests, and every unexplained febrile illness should be properly investigated for possible tuberculous foci in the lungs or elsewhere.

Severity of Diabetes / TB in coexistence

In the series of Jha et al[35] 51.7 percent of their cases were severely diabetic while 48.3 percent of cases had far advanced tuberculosis. As per the reports of Holden & Hiltz[37] (1962) Nihalani[38] et al (1978) and Goyal[39] et al (1978) the tuberculosis was far advanced in the diabetic they had studied. The comparable severity in diabetic state and the advanced lesion in the lungs were reported by various authors; Deshmukh[40] et al (1966) in 40.34 percent, Nanda and Tripathy[41] (1968) in 54.2 percent, Nihalani[38] et al (1978) in 48.3 percent, severity of pulmonary tuberculosis have been assessed according to criteria laid down by the National Tuberculosis Association of U.S.A. 1961.

Incidence by age

Tuberculosis in the general population has a higher incidence with increasing age. Fitz[42] reported the incidence of tuberculosis is higher in the elderly diabetics. This has been a constant finding in almost all the reports and maximum incidence is seen around forty years. Roy Chowdhary and Sen[28] reported from Calcutta maximum incidence in the age group 25-54 years, where as Jha et al[35] in 1980 from Bokaro reported a peak incidence in the age group of 41-50 years.

Racial and gender difference

Old concept that Negroes were immune to diabetes mellitus is false. The studies done by Joslin after analyzing the death rates of Whites and Negroes who were Industrial Policy holders of Metropolitan Life Insurance Company proved that there was definitely a higher incidence of diabetes among Negroes as compared to the White irrespective of the sex. Similarly tuberculosis had a fulminating course in Negroes with higher mortality ratio. But the prevalence rate is low. Boucot[43] found in the Philadelphia Survey that the tuberculosis prevalence was 10 percent among the 2245 diabetic whites when compared to 4.3 percent of the 861 diabetic Negroes. In 1955 the mortality rate as per Philadelphia Diabetic Survey were 25.3 per 10000 for white males and 4.6 for white females compared with Negroes 54.7 per 10000 for non-white males and

36.7 non-white females. Increased prevalence of diabetes in tuberculosis patients was noted in studies from western workers, other workers and as well as Indian workers.

As in the general population the males are more affected by tuberculosis in patients with diabetes. Diabetes has also been associated with a progressive shift of male predominance in pulmonary TB. Definite male preponderance in incidence is noted and is well comparable to the incidence of DM and TB in general population.

Radiological aspects

Lower lung field tuberculosis was significantly associated with patients older than 40yrs, in females more than males and was more frequently observed in diabetes (Basuglo[44]et al in Respiration 2001).

Ezung T[45], et al from (Imphal) found that the Type 2 diabetic tuberculosis patients were above 40 yrs and 11 out of 27 patients had minimal lesions, 7 had moderate lesion, and 9 had far advanced lesion, Cavitation in 3, and fibrosis in 4 patients.

Diabetes mellitus does not affect the presenting features of pulmonary tuberculosis and the clinical presentation of TB in diabetic patients is similar to

that in non-diabetic patients and the radiographic findings have been described as both typical and atypical.

Some studies have suggested an increased frequency of lower lobe TB as well as a greater predisposition to cavitary disease. The possibility of the pulmonary lesion being predominantly associated with lower lung field diseases in older patients makes it difficult to diagnose and evaluate accurately if this is not borne in mind.

However, studies by Parmer and Berger have shown that lower lung field involvement is an infrequent location of pulmonary TB, occurring in 7% or less of patients with active pulmonary TB.

Since the association of diabetes only and none of the other factors were found to be statically significant, atypical radiographic presentation should be first investigated for the presence of diabetes.

A significant observation of relevance is by Morris et al[46] who found multiple lobe involvement as the predominant presentation of pulmonary tuberculosis in diabetics.

Immunological aspects

Tsukaguchi[47] et al were the first to demonstrate the production of cytokines interleukin – 1 beta (IL-1 beta) TNF alpha and IL 6 by peripheral monocytes of patients with pulmonary tuberculosis and diabetes. They observed that

1. The production of IL-beta, TNF alpha, and IL-6 in tuberculosis patients were higher than that of observed in the healthy control subjects.
2. But there were significantly lower levels in those with Diabetes mellitus with pulmonary tuberculosis.
3. The production of IL-1 beta and TNF alpha in patients of DM and tuberculosis with poor control of Diabetic state was significantly lower than that observed in patients with good control.
4. The TNF alpha production had significantly inverse-correlation to HbA_1C in patients with diabetes and tuberculosis.

Tsukagudi[47] et al continued the pioneering work of cytokines in patients of tuberculosis, to define the immunopathologic mechanisms in patients with DM and TB, the production of IFN- gamma by CD_4+T cells, and the patients were followed up longitudinally during antituberculous chemotherapy. At the time of diagnosis, IFN gamma production of CD_4+T cells in either tuberculosis patients without DM (TB) or with DM was significantly lower than that in the

healthy control CD_4+T cells in tuberculosis patients with DM under poor control. They produced significantly less IFN-gamma than did patients with DM under good control. In longitudinal studies, IFN-gamma production in tuberculosis with good control diabetic patients returned to the control level by 6 months, whereas the production in TB with poor control diabetic patients remained depressed. There was no significant relation between regimens of antituberculous chemotherapy and the production of IFN-gamma in all subject groups. IFN-gamma production was depressed in TB with poor control diabetic patients treated with ATT for 6 months. These results indicate that depressed production of IFN-gamma in TB with poor control diabetic patients is prolonged not due to tuberculous infection but by intrinsic defect presumably induced by poorly controlled DM.

Theories for conjoint presence of TB & DM

Although diabetic patients, as a group, are more susceptible to tuberculosis, there is no clear explanation as to why they are more susceptible. A probable cause for increased incidence of pulmonary tuberculosis in diabetic could be defects in host defenses and immune cell function.

Immune derangements predominately involve the cell mediated arm of the immune system. Also, the degree of hyperglycemia has been found to have a distinct influence on the microbicidal function of macrophages, with even

brief exposure to blood sugar level of 200mg% significantly depressing the respiratory burst of these cells. This is borne out of the observation that in poorly controlled diabetics, with high levels of glycosylated haemoglobin, tuberculosis follows a more destructive course and is associated with higher mortality. Multiple pulmonary physiologic abnormalities have also been documented in diabetics that contribute to delayed clearance of and spread of infection in the host. Infection with tubercle bacilli leads to further alteration in cytokines, monocyte macrophages and CD_4/CD_8 T cell populations. In summary, various factors have been attributed as causes for the wide prevalence of coexisting pulmonary tuberculosis and diabetes such as:

Diabetic autonomic neuropathy leading to abnormal basal airway tone due to an alteration in vagal pathways and thus causing a reduced bronchial reactivity and bronchodilation is considered as one of the probable causes. The others are:

Low Opsonic index, Decreased bactericidal activity, Lowered tissue resistance, Decreased synthesis of collagen, Impaired defensive function of RE cells, Increased availability of glycerol in tissues that act as substrate for TB bacilli, Lack of adequate substrate for antibody formation due to disturbed protein metabolism. Presence of gastroparesis causing varying degrees of impaired gastrointestinal drug absorption.

Hyperglycaemic state influencing sub optimal tissue levels of medications or interfering with alveolar macrophage and CD_4 cell function. Lowered production of interleukin -1 beta and tumor necrosis factor – alpha by peripheral blood monocytes.

Abnormal chemotaxis, adherence, phagocytosis and microbicidal function of polymorphonuclear cells. Decreased peripheral monocytes with impaired phagocytosis. Poor blast transformation of lymphocytes. Defective C3 opsonic function.

Acute severe stress is an important cause of the development of impaired glucose tolerance. Impaired glucose tolerance in tuberculosis is much higher than overt diabetes. Various Indian studies have estimated the prevalence of glucose intolerance in tuberculosis to be 1.5% to 14%.

Although IGT reverts to normal in a large number of cases with effective chemotherapy, the higher percentage with IGT is significant because, according to the National Diabetes Data Group of NIG, 1 to 5% of patients with IGT may progress to overt diabetes, annually.

Theories of glucose intolerance in TB

Theories have been put forward to explain why tuberculosis patients develop glucose intolerance. Bloom (1969)[48] suggested that occult glucose

intolerance predisposes to diabetes. Zack et al[49] (1973) suggested that glucose intolerance was not merely a reaction to acute tuberculous infection but rather a prediabetic state. Hadden[50] (1967) suggested malnutrition in tuberculosis as a possible cause. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon and cortisol which raise the blood sugar level (Guptan et al, 2000)[51].

Roy Choudhary and Sen (1980)[52] suggested tuberculosis of pancreas as the possible cause. Similarly, higher incidence of chronic calcific pancreatitis occur in patients of diabetic pulmonary tuberculosis leading to absolute or relative insulin deficiency state (Mollentz et al, 1990)[53] Clinical and sub clinical hypoadrenalism has been described in these patients (Guptan and Shah, 2000)[51]. Plasma level of IL -1 and TNF –α are also raised in severe illness, which can stimulate anti-insulin responses. Age, co-existing illness and alcoholism also influence the host response (Fernandez et al, 1997)[54].

Course of Tuberculosis in diabetes Patients

Studies reviewing their conjoint association have shown that uncontrolled diabetes predisposes towards the development of tuberculosis, but effectively treated diabetics were no more liable for tuberculosis infection than non- diabetics. Insulin deficiency results in impairment of both leucocyte and

lymphocyte mediated responses to infection that improve with antidiabetic treatment.

Diabetes reactivates latent tuberculosis. Studies have shown that the risk is 2 to 6 times higher than in patients without diabetes. With regard to relapses, it is learnt that the degree of control of Diabetes mellitus did not influence the relapse rates but when relapses occurred, resistant strains were more often encountered in diabetics.

There is no evidence that treatment of active tuberculosis in patients with diabetes is less effective than it is in patients without diabetes.

Clinical aspects of concomitant Diabetes and Tuberculosis

Patients of tuberculosis who develop diabetes have greater clinical severity at the onset, a greater degree of lung involvement and residual changes.

The diabetics who develop pulmonary tuberculosis have higher blood sugar levels and develop complications like coma and diabetic microangiopathies.

Diabetic patients, who develop chest symptoms, need increasing insulin requirements or present with accelerated weight loss should prompt investigations to rule out co- existent pulmonary tuberculosis.

Few studies have attempted to determine the presentation difference and the differential risks of developing tuberculosis among patients with Type 1 versus Type 2 diabetes. Swai et al[55] in Tanzania followed 1250 patients with diabetes and noted that 5.6% patients developed tuberculosis. This study showed that the prevalence of tuberculosis was greatest in:

The young,

Those with low body mass, and

Those with Type 1 DM occurring in 8.8% compared to 2.7% of Type 2 DM cases,

Vulnerability of Type 1 diabetes mellitus is amply evidenced in many reports form many parts of the world. The 10 year actual risk of acquiring tuberculosis was 24.2% for 116 Type 1 diabetes mellitus and 4.8% for the rest in one study form Chile.

Tuberculosis in Type 2 Diabetes is not uncommon either, as 5 – 10% have pulmonary tuberculosis in developing countries. Though tuberculosis is more prevalent in Type 1 diabetes mellitus, the magnitude of the problem in Type 2 diabetes mellitus should be considered with no less concern in the purview of Type 2 diabetes mellitus, affecting an overwhelming larger number

of people and also emerging as a serious public health problem in developing countries.

Challenges in therapeutics

A study by Bashar M et al has revealed that the proportion of cases of MDR – TB was significantly higher in patients with coexisting diabetes mellitus and this number was constant over years. But scientists who performed a study in a tertiary care teaching hospital in South India to evaluate the association of drug resistant tuberculosis in diabetic subjects have concluded that diabetic tuberculosis patients do not have an increased risk of mycobacterial drug resistance. The researchers also concluded that drug resistance to first line anti-TB drugs was not found to be associated with diagnosis or duration of diabetes mellitus.

Rifampicin is a powerful inducer of the hepatic microsomal enzyme system and frequently interacts with other drugs, especially antidiabetic medications. It lowers the serum levels of sulphonylureas and biguanides. Hence patients with co – existing diabetes should have their doses of oral antidiabetic drugs adjusted upwards according to plasma glucose concentration.

Takayasu et al observed that Rifampicin induced an early phase hyperglycemia which he attributed to augmented intestinal absorption and accelerated metabolism of oral hypoglycemic agents.

Rifampicin is known to cause early hyperglycemia in non-diabetic patients with or without pulmonary tuberculosis, and also to augment intestinal absorption of glucose.

Rifampicin accelerates the metabolism of anti-diabetic drugs and thus, per se may increase insulin requirements.

Isoniazid antagonizes sulphonylureas and impair insulin release and action, and Rifampicin shortens the plasma half life of sulphonylureas.

The earliest study of DM in pulmonary tuberculosis was done by Nichols[56], and he postulated that a reciprocal relationship should be expected when these two disease entities co-exist. Some amount of glucose intolerance predisposes to tuberculosis and some underlying endocrine abnormality predisposes to latent diabetic state and tuberculosis. Roy Choudhary and Sen[52] suggested that tuberculosis of pancreas may give rise to glucose intolerance.

Irrespective of the triggering mechanism(s), the fact remains that an epidemic of diabetes mellitus is sweeping the country. The recent prevalence data has propelled the estimates for India upwards-32million in 2000 and 80million in 2030. India is also the home to the largest number of tuberculosis patients[22].

Type 2 diabetes is increasing worldwide and India is mentioned as diabetic capital in the diabetic map, and the reason being multifactorial. Even in the institution of free supervised and unsupervised multi drug chemotherapy the pulmonary tuberculosis so far could not be contained successfully.

The possibility of the disease entity emerging itself with different clinical presentation eg. non cavitary pulmonary tuberculosis especially in the younger age group and in the elderly has been thought of. The multi drug resistance itself is a threat and in a situation like that of Indian scenario with increasing incidence of Type 2 diabetes, and with the phenomenon of multi drug resistant cases propping up, a serious consideration and a meaningful approach to the problem, and an attempt for an early diagnosis is absolutely mandatory to look for the possibility of diabetes in freshly detected tuberculosis patient and in those on treatment with ATT. All tests to confirm or exclude diabetes mellitus should be done as is done in those for the assessment of HIV status of the pulmonary tuberculosis patient as a routine.

The clinician should suspect diabetes in TB patients, when symptomatic improvement is not gained with ATT and should treat diabetes aggressively if it is detected.

From the literature available, it is to understand that the association of Diabetes mellitus Type 2 with pulmonary tuberculosis is a fact and not a fallacy.

RELATED STUDIES

1. Pulmonary tuberculosis in diabetics

By Morris JT. Seaworth BJ Mc Aelister CK. Chest 1992 Aug 102 (2)539-41[46].

In diabetes, it has been suggested that tuberculosis tends to occur predominantly in lower lobes. Multiple lobe involvement was the predominant chest roentgenographic finding in Diabetes with Pulmonary Tuberculosis.

2. Does diabetes alter the radiological presentation of pulmonary tuberculosis

Shaikh MA. Singla R, Khan NB, Sharif NS, Saigh MO. Chest 1994 Jul 106 (1) : 326[57].

Pulmonary tuberculosis with diabetes mellitus group are more likely to present with atypical radiological images.

Among diabetic patients presenting with lower lung field lesions or cavities possibility of tuberculosis should always be considered for prompt diagnosis and management.

3. Tuberculosis and diabetes

D.C. Lahiri and P.K. Sen (From B.C. Roy Research Institute, Calcutta). Indian J. Tub.Vol. X, XI, No.2, 1974[58].

The prevalence of diabetes is 6.5% in tuberculosis population.

4. Pulmonary tuberculosis and diabetes

P.A. Desh Mukh and T.Shaw Ind. J. Tub. 1984, 31, 114[59].

The incidence of tuberculosis in DM was 5.6%. Routine post breakfast urine sugar or blood glucose examination should be done in all pulmonary tuberculosis patients to find out association of DM.

5. Diabetes mellitus and pulmonary tuberculosis

S.R. Tripathy et al Ind. J. Tub. 1984, 31, 122[60].

The prevalence of pulmonary tuberculosis is 4.1% of known diabetic patients. The prevalence of diabetics among pulmonary tuberculosis patients is 3%.

6. Prevalence of diabetes mellitus among patients with pulmonary tuberculosis

Research committee of tuberculosis association of India. Ind. J. Tub. 1987, 34, 91[61].

The prevalence of DM among tuberculosis patients is considerably higher than general population. The rate is higher in patients above the age of 40.

7. DM – TB – The brewing double trouble by Lalit Kant.

Ind. J. Tub. Vol 50No.4, Oct. 2003[62].

8. Older Studies

Banyai (1931) reported that 0.59 per cent of 5.225 tuberculous admissions were found to have diabetes[63].

Wiener and Kavee (1936) reviewed previous incidence of 0.25 per cent to 0.66 per cent diabetes among tuberculous patients, although they reported that 6.4 per cent of their own 3,385 tuberculous admissions had diabetes[64].

Rest (1941) reported an incidence of 0.025 per cent diabetes in 1,360 tuberculosis admissions in a sanatorium for Jewish patients[65].

Israel and Payne (1940) found 2 per cent diabetes among 610 tuberculous patients[66].

Banyai and Cadden in 1944 reviewed previous reports concerning the incidence of diabetes among tuberculous patients showing rates of 0.31 percent in 4,500 patients (**Tompkins** 1929) 0.7 per cent in another 3,963 patients (**Banyai** 1931) and 1.6 per cent in 5,575 patients in a 13 – year study of their own[67].

Among 2,366 tuberculous admission in the city of Honston Tuberculosis Hospital in the period 1940 to 1950, only 0.63 per cent were found to have diabetes (**Speck et al** 1952)[68].

Ferrara (1952) found 2.1 percent diabetes among, 178 tuberculous admissions form 1937 to 1950[69].

Reaud (1953) cited previous rates of 0.17 to 1.6 percent diabetes among tuberculous patients and 0.98 percent diabetes among 3,850 sanatorium admission from 1950 to 1952. However, he referred to one of the highest rates of diabetes, reported in tuberculous patients – 14.23 percent diabetes among predominantly Jewish patients in Montefiore Hospital in New York[70].

Nichols (1957) conducted diabetic screening in the form of a modified glucose tolerance test on 305 subjects. 178 of these subjects comprised of a uniform group of young otherwise healthy military men hospitalised for tuberculosis. Follow up testing showed that 22 per cent of later group presented various abnormalities of glucose tolerance and that at least 5 per cent were mild diabetic. Although these figures probably indicated the maximal incidence of diabetes in the group examined, but if other accepted criteria for the diagnosis of diabetes were substituted for the criteria used here, then the incidence of diabetes might be listed as 9 per cent, 11 per cent or 18 per cent rather than 5 per cent[56].

Table 2: Impaired glucose tolerance tests in patients of pulmonary tuberculosis

Author	Year	No. of tubercular patients	Prevalence of diabetes /IGTT
Khanna[71]	1968	150	6.6%

Bloom[5]	1969	47	34%
Kishore et al[72]	1973	90	20.9%
Zack et al[49]	1973	256	41%
Lahiri and Sen[58]	1974	851	66%
Roychoudhary et al[52]	1980	961	27.25%
Marais[73]	1980	436	2.1%
Gulbas et al[74]	1987	30	13.3%
Olyboyo and Erasmusl[9]	1990	54	3.7%
Mugusi et al[75]	1990	506	6.7%
Jawad et al[76]	1995	106	49%
Fernandez et al[54]	1997	300	9.3%
Lin et al[77]	1998	-	4.86%
Basoglu et al[44]	1999	58	19%
Chukanuva et al[78]	2000	69102	0.34%
Yamagishi et al[79]	2000	4169	14.1%
Firsova et al[80]	2000	130	10.8%
Guptan and Shah[51]	2000	-	9.7%
MK Jain et al[81]	2003	106	16.98%

Gajanan Gavde[82], in his clinical review gives the comparative proportions of pulmonary tuberculosis found in diabetics and diabetes found in cases of pulmonary tuberculosis by different authors.

Table 3

Authors	**PT in DM%**	**DM in PT%**

Jamaica report		0.9
Patel et al[36]	5.7	-
Deshmukh et al[40]	8.3	-
Philadelphia report[43]	8.4	-
Ross	30.0	20.0
Chittaranjan Kal et al	24.2	-
Nichols[56]	-	22.0
Bahulkar et al	-	26.3
Roy Choudhary et al[52]	-	27.2
Holden Hiltz[37]	45.3	37.7

PT – Pulmonary tuberculosis, DM – Diabetes mellitus

AIM

- To assess the prevalence of diabetes and IGT among newly detected young sputum positive tuberculosis patients.

- To assess the radiological profile of such cases.

- To analyze the gender difference.

- To suggest workable guidelines to detect diabetics mellitus among tuberculosis population.

MATERIALS AND METHODS

Type of study : Cross sectional study

Setting : Dept of Medicine, GRH, Madurai.

Collaborating Dept. : Dept. of Thoracic Medicine,

Dept. of Diabetology

Duration of study : 1 year August 2005 – July 2006

Ethical Clearance : Obtained, a copy is enclosed in annexure I

Consent : Informed consent was obtained

Inclusion criteria : Newly diagnosed young (age 25-45) sputum positive tuberculous patients of both sexes who were conscious cooperative and free of overt comorbid illness were considered for the study.

Exclusion criteria : Patients who had any of the following were excluded from the study.

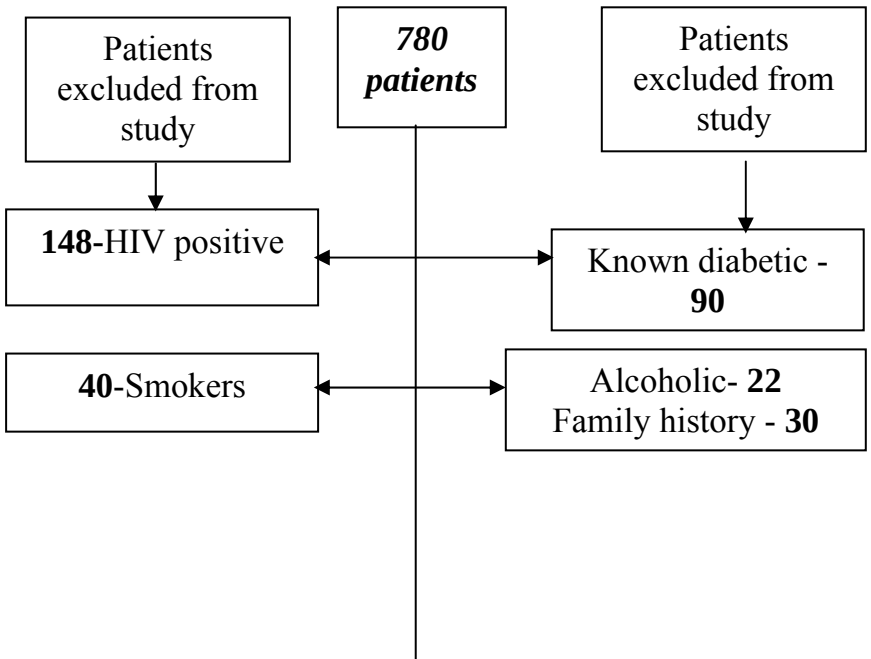
1. Age <25 - > 45
2. HIV positive
3. Known diabetic
4. BMI >25
5. Hypertensives
6. Patient with thyroid or adrenal disorders
7. Acute conditions
    a. Acute myocardial infarction
    b. Acute CVA
    c. Acute medical emergencies
8. Patients with malignancy
9. Bed ridden patients
10. Psychiatric patients

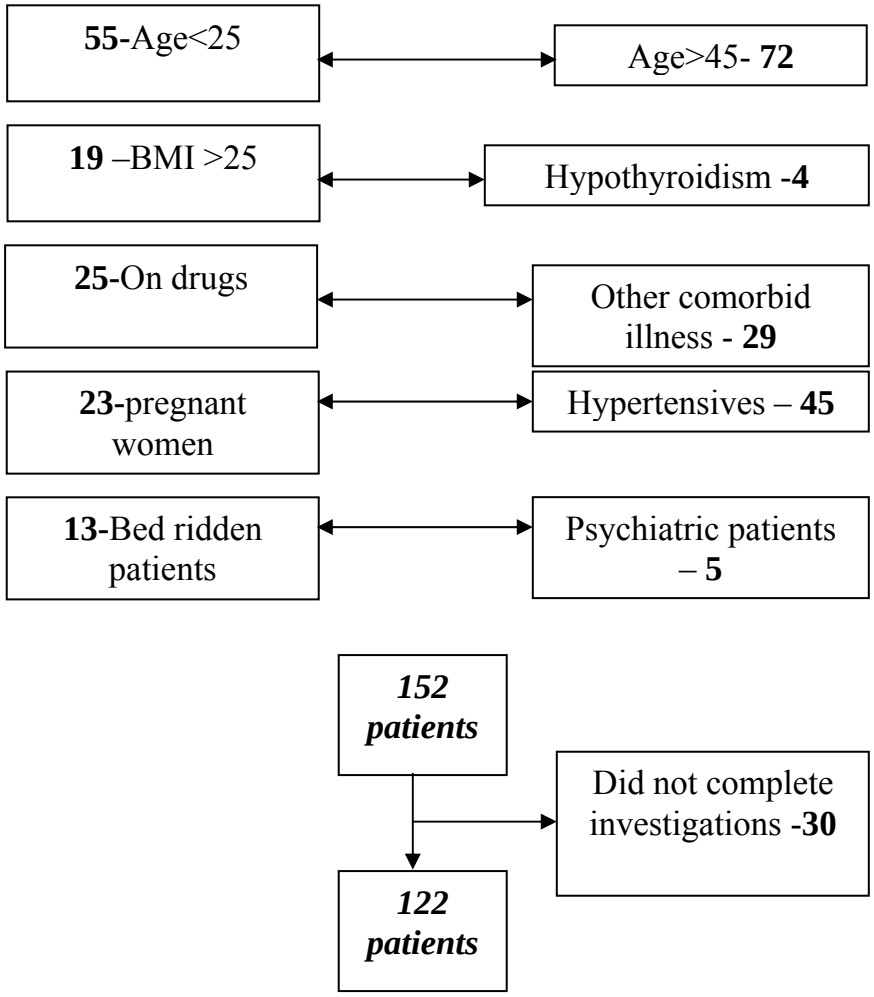
8. Uncooperative patients
9. Pregnant women
10. Women on oral contraceptive pills
11. Patients who are alcoholic / smokers
12. Patients who are on drugs-steroids, β blockers diuretics etc
13. Family history of diabetes

MATERIALS

A total of one hundred and twenty two consecutive patients of newly diagnosed young sputum positive tuberculosis patients attending the outpatient clinic of Department of Thoracic Medicine GRH, Madurai were included for this present study on the basis of a set of inclusion and exclusion criteria out of 780 patients seen. The exclusion of other patients is given in figure 1 below.

Figure 1: Patient flow chart





METHODS

Selected sociodemographic, laboratory and radiological data were elicited from these patients and recorded in the proforma.

1. **Socio demographic data**

   - Age
   - Sex

- Domicile – Rural / Urban

2. **BMI**
3. **Radiological data**

   Chest X ray of all patients were taken and reports included.

4. **Laboratory Data**

   - GTT – was done in all patients. Blood sugar was measured using COBAS autoanalyser.
   - Sputum for acid fast bacilli by Ziehl Nielsen technique.

5. **Conflict of interest** – Nil
6. **Financial support** – This study did not receive any financial support from any organization
7. **Statistical analysis** – Data were entered in a predetermined proforma and later entered into a Microsoft excel spread sheet and analysed using chi square test and t test.

LIMITATIONS OF THE STUDY

1. As the inclusion criteria were rigid, the true numbers of cases will be more than the number of cases reported daily during the study period.

2. HbA_1C could not be done due to technical constraints.

3. Follow up of patients in IGT-group was not done because of practical difficulties.

4. Target organ damage assessment of those patients detected with diabetes was not done as they were beyond the scope of this study.

DEFINITIONS USED FOR THE STUDY PURPOSE

1. Sputum positive tuberculosis (RNTCP guidelines)

Patients with at least 2 sputum samples positive for AFB by microscopy and those with one sputum sample positive and radiological abnormalities consistent with active pulmonary tuberculosis.

2. Age definition by WHO

Young	25-45
Middle age	45-65
Elderly	>65

3. OGTT[7]

The OGTT should be administered in the morning after the patients had had at least 3 days of unrestricted diet (>150 g of carbohydrate daily) and usual physical activity. The test should be preceded by an overnight fast of 10 to 16 hours, during which the patient may drink water. The patient may not smoke during the test. Factors that may influence interpretation of the results of the test should be recorded (e.g., medications, inactivity, infection). Such factors should be taken into account in interpreting the results of the test.

After the fasting blood sample is collected, the subject should drink 75g of anhydrous glucose (or partial hydrolysates of starch with an equivalent carbohydrate content) in 150 to 300 of water over the course of 5 minutes. Blood samples are drawn before (fasting) and 2 hours after the load.

4. ADA 2003 recommendations of hyperglycemia[7]

Categories of Hyperglycemia According to Venous Plasma Glucose Concentrations.

Table 4

Fasting Plasma Glucose Level				
	Normal	**Impaired**	**Diabetes**	
2-Hour postload	<100mg/dl	100-125 mg/dl	≥126 mg/dl	Not done

plasma glucose level	<5.5 mmo1/L	5.6-6.9 mmol/L	≥ 7.0 mmol/L	
<140 mg/dl (<7.8 mmol/L)	Normal	IFG	Diabetes	Normal
140-199 mg/dl (7.8-11.0 mmol/L)	IGT	IFG/IGT	Diabetes	IGT
≥ 200 mg/dl (≥11.1 mmol/L	Diabetes	Diabetes	Diabetes	Diabetes
Not done	Normal	IFG	Diabetes	Unknown

5. BMI = $\frac{\text{Weight}}{(\text{Height in m})^2}$

6. X-ray Zones –

- Upper Zone - 1st and 2nd intercostal space
- Mid Zone - 3rd and 4th intercostal spaces
- Lower Zone - Rest of intercostal spaces

RESULT ANALYSIS

Table 5

Distribution of cases in relation to Age

Age	Male	Female	Total
25-30	19	16	35
31-35	12	8	20
36-40	16	7	23
41-45	34	10	44

Total	81 (66.39%)	41 (33.6%)	122

Study group contains 66.39% Males and 33.6% Females. Age and gender wise analysis of the study population shows males are more affected with TB than females. 36% of the study population falls in the 41-45 age category indicating increased incidence of sputum positive TB in that age group.

Table 6

Statistical Analysis of age and gender

	Male	**Female**	**Total**
Mean	37.19	34.20	36.81
SD	6.57	7.06	6.86
Range	25-45	25-45	25-45

Blood Sugar Analysis

Out of 122 patients studied, 57 had normal blood sugar, 6 patients had IFG, 38 had IGT, 21 had DM, as per the ADA Grading of OGTT results.

Table 7

GTT Results

ADA	Male	Female	Total
N	36 (29.5%)	21(17.21%)	57(46,72%)
IFG	3(2.4%)	3(2.4%)	6(4.9%)
IGT	27(22.13%)	11(9.0%)	38(31.14%)
DM	15(12.29%)	6(4.9%)	21(17.21%)

This study revealed that 53.28% of the patients had abnormal blood sugar values in the form of IFG – 4.9% IGT – 31.14% DM-17% where as prevalence of IGT in normal population in Tamilnadu – was 14% and DM was 13.4% (Ramachandran et al)

Table 8

Statistical analysis of IGT results

ADA Grade	Proportion		t value	p value
	Study Group	Normal Population		
IGT	0.3115	0.1400	3.1507	0.0011
DM	0.1721	0.1350	0.7683	0.4431

The IGT in the study group was higher than the normal population with definite statistical significance $p < 0.05$. But Diabetes in the study group didn't show any statistical significance when compared normal population $p > 0.05$.

Table – 9

	IGT	**DM**
Proportion	0.3115	0.1721
P	0.0106	

This table shows that the prevalence of IGT is more than diabetes in the study group and p value significant $p = 0.0106$.

Result of OGTT were further analyzed on the basis of Age / Gender

Age wise analysis

Table 10

Age wise analysis of OGTT results

Age Group	**ADA Grade**			
	N	**IFG**	**IGT**	**DM**
25-30	23	3	7	2

31-35	8	1	10	1
36-40	13	0	8	2
41-45	13	2	13	16
Total	57	6	38	21

Analysis of age in different groups with reference to the GTT results revealed that 55.2% of IGT (n=38) and 85.7% of DM (n=21) occurred in the 36-45 age group showing that increased coexistence of TB and IGT and DM in this age group.

Table - 11

Gender wise Analysis

ADA Grade	Male	Female	Total
N	36	21	57
IFG	3	3	6
IGT	26	11	38
DM	15	6	21
Total	81	41	122

Table - 12

Age and Gender wise Break up of OGTT results

Age	Males				Females			
	N	IFG	IGT	DM	N	IFG	IGT	DM
25-30	12	1	5	1	11	1	2	1

31-35	5	1	5	1	3	0	5	0
36-40	9	0	5	2	4	0	3	0
41-45	10	1	12	11	3	1	1	5

Table - 13

Statistical Analysis of Gender difference of DM / IGT

	M	**F**	**P**
DM	0.1852	0.463	0.5804
IGT	0.3311	0.2683	0.4551

There is no statistically significant difference in the IGT, or DM among males / females and P value > 0.05 in significant.

Analysis of Radiological Finding

Table 14

X – Ray Zone involvement

Zone	**Right**			**Left**		
	M	**F**	**Total**	**M**	**F**	**Total**

Upper Zone	35	21	56	29	11	40
Mid. Zone	3	0	3	1	1	2
Lower Zone	2	4	6	3	1	4
Multiple Zone	10	2	12	7	3	10

Table 15

Correlation of X-ray zone involvement with GTT results

Zone	N	IFG	IGT	DM
Upper Zone	34	3	28	10
Mid. Zone	3	0	0	2
Lower Zone	4	2	3	1
Multiple Zone	9	1	5	7

61% of the study group showed upper zone involvement and when correlated with GTT results. 59% of N (n=59) 50% of IFG (n=6), 73.6% IGT (n=38) and 47.6% of DM (n=21) cases showed upper zone involvement.

Table 16

Statistical Analysis of X-ray zone involvement (Upper zone) – correlated with IGT and DM

	Male	Female	Total
DM	0.1406	0.1250	0.1354

IGT	0.3750	0.3438	0.3646
P	0.0021*	0.0365*	0.0002*

This clearly shows that upper zone lesion predominate in both IGT and DM in both genders and the p value is statistically significant p(< 0.05).

Table 17

Analysis of Lesions in chest X-ray

Lesions	Right	Left	Total	Percentage
Infiltrate	61	41	102	72.34%
Consolidation	6	3	9	6.38%
Cavity	18	3	21	14.89%
Effusion	5	2	7	4.96%
Hydropneumothorax	2	2	4	2.13%
Total	92	51	142*	

* Total no of lesions is more than sample size because multiple lesions were observed in some patients. Infiltrates were the commonest lesion documented (72.34%) in the study group.

Table - 18

Analysis of lesions in X-ray according to Age – Right

Age group	Infiltrates	Cavity	Consolidation	Effusion	Hydropneumothorax
25-30	18	4	1	0	1

31-35	12	1	1	2	0
36-40	7	5	2	2	0
41-45	24	8	2	0	1
Total	61	18	6	4	2

Table - 19

Analysis of lesions in X-ray according to Age – Left

Age group	Infiltrates	Cavity	Consolidation	Effusion	Hydropneumothorax
25-30	12	2	3	0	0
31-35	4	0	0	1	0
36-40	9	1	0	0	0
41-45	16	0	0	1	1
Total	41	3	3	2	1

Analysis of lesion according age group shows that infiltrates are common in all age group when compared to other lesions.

Table - 20

Analysis of lesions according to blood sugar values – Right

Lesions	ADA Grade			
	N	IFG	IGT	DM
Infiltrates	27 (62%)	2 (50%)	23 (74%)	9 (64%)

Cavity	10 (25%)	1 (25%)	3 (9%)	4 (28%)
Consolidation	4 (9%)	0	1 (3%)	1 (7%)
Effusion	2 (4%)	0	3 (9%)	0
Hydropneumo Thorax	0	1 (25%)	1 (3%)	0
Total	43	4	31	14

Table 21

Analysis of Lesions according to Blood Sugar value – Left

Lesions	**ADA Grade**			
	N	**IFG**	**IGT**	**DM**
Infiltrates	16 (76.4%)	3 (100%)	14 (82%)	8 (80%)
Cavity	1 (4.7%)	0	1 (5.8%)	1 (10%)
Consolidation	3 (14.2%)	0	0	0
Effusion	1 (4.7%)	0	1 (5.8%)	0
Hydropneumothorax	0	0	1 (5.8%)	1 (10%)
Total	21	3	17	10

Infiltrates dominate as the major lesion in all the ADA grades as shown in the Tables above

Table – 22

Domicile

ADA grade	**Urban**	**Rural**	**Total**
Normal	15	42	57

IFG	4	2	6
IGT	30	8	38
DM	15	6	21
Total	62	60	122

62 of the study population belonged to urban domicile and 60 to rural domicile. 79% of urban population had abnormal results [IFG – 6.4%, IGT – 48.3%, DM – 24.19%] when compared to 26.6% in rural population.

Table 23

Statistical analysis of Rural Urban Variation

	Urban	Rural	t value	p value
IGT	0.4516	0.1667	3.5873	0.0005*
DM	0.2419	0.1000	2.1257	0.0356*

The statistical analysis shows that both IGT and DM were common in urban population with the significant p value < 0.05*.

Table 24

Statistical analysis of BMI

	Male	**Female**	**Total**

Mean	22.74	22.08	22.76
SD	2.00	1.47	1.83
Range	20-24	20-24	20-24

Mean BMI was slightly above the predicted BMI of South Indian population (18-22). Statistical analysis among ADA grades didn't show any significant difference p value was > 0.05.

DISCUSSION

Tuberculosis is a highly prevalent disease in developing countries – particularly in India. Among Indian population it is estimated that 1-2% of

population are suffering from tuberculosis. Diabetes mellitus is also increasing among Indian and Asian population and WHO estimates that 30 millions of Indians will have diabetes by 2025 and current prevalence of diabetes mellitus in Tamilnadu is about 14%.

Already various reasons for predisposition of individuals to tuberculosis as well as diabetes mellitus have been described. Now it is clear that diabetics are prone for tuberculosis hence periodic studies on their association will help us do find out the changing trends.

Present study analyses OGTT results in tuberculous patients. 31.14% had IGT and 17.2% had DM and the total number of patients with abnormal blood sugar values (IFG, + IGT + DM) account for 53.28% of the study group. Recent studies over the past 5 years have shown variable results for IGT in TB.

Table 25

Recent studies showing IGT prevalence in TB

Study	No. of Pts	Prevalence of IGT

Chukanava et al (2000)[77]	69102	034%
Yamagishi et al. (2000)[78]	4169	14%
Firsova et al (2000)[79]	130	10.8%
MK Jain et al (2003)[80]	136	16.98%
Present study	122	31.14%

Various authors have suggested the mechanisms of impaired glucose tolerance among tuberculous patients.

Bloom (1969)[48] suggested that occult glucose intolerance predisposes to diabetes. Zack et al[49] (1973) suggested that glucose intolerance was not merely a reaction to acute tuberculous infection but rather a prediabetic state. Hadden[50] (1967) suggested malnutrition in tuberculosis as a possible cause. Acute severe stress, fever, inactivity and malnutrition stimulate the stress hormones epinephrine, glucagon and cortisol which raise the blood sugar level (Guptan et al, 2000)[51]. Clinical and sub clinical hypoadrenalism has been described in these patients (Guptan and Shah, 2000)[51]. Plasma level of IL -1 and TNF –α are also raised in severe illness, which can stimulate anti-insulin responses. Age, co-existing illness and alcoholism also influence the host response (Fernandez et al, 1997)[54].

The increased prevalence of IGT in the present study can be explained by increase in IGT among general population due to reasons like urbanization,

sedentary life style, eating habits etc. But the IGT is significantly high in TB population -31% when compared to 14%in normal population and p value is significant <0.05

The present study shows that IGT in tuberculosis patients is two times higher than general population.

The prevalence of diabetes mellitus found in this study is 17.21% and is high compared to 13% in the general population of Tamilnadu belonging to the same age group; even through the p value is not significant.

In view of the increased prevalence of diabetes mellitus in tuberculosis population it is suggested that all tuberculosis patients should be evaluated clinically and biochemically for diabetes mellitus as detection and control of diabetes mellitus will help to achieve better tuberculosis control.

Table 26

Age group in relation to GTT results

Age	IGT	DM
25-35	44%	14.3%

36-45	55.3%	85.7%

Present study also reveals an important point that IGT was almost equally distributed in the study population regardless of age, whereas DM, was more in >35 age group . It can be derived from these results that prevalence of IGT is increasing among young Indian population, and is also significantly more among the tuberculous patients and they should be followed up as 50% of patients in the IGT group will develop diabetes. IGT is a well established risk factor for diabetes and coronary artery disease and this fact should be kept in mind.

Of the diabetics detected in this study, 85.7% were above 35 years of age, and the fact that advancing age, favors the coexistence of diabetes and tuberculosis is again proved here.

Male patients were almost twice the number of female patients in this study (81 vs 41). The gross variation of increased male prevalence for tuberculosis may be related to their increased exposure to tuberculosis and habits like smoking leading to increased susceptibility. Also alcoholism which leads to under nutrition and suppression of immune system may contribute to this malady. But the GTT results didn't show any significant variation according to gender in this study.

Radiological manifestations

Considering the zone of tuberculosis involvement in the study group upper zone involvement was predominant, regardless of the glycaemic status.

61% of the study group shows upper zone involvement. According to ADA grade, upper zone inv in this study is as follows.

Table 27

Upper zone involvement

ADA Grade	Upper zone involvement	Percentage	Total
N	34	59	59
IFG	3	50	6
IGT	28	73.6	38
DM	10	47.6	21

As far as the lesions are considered, infiltrates were the commonest lesion observed in the study group regardless of blood sugar values.

Table 28

Percentage of infiltration

ADA Grade	Right %	Left %
N	62	76.4
IFG	50	100
IGT	74	82
DM	64	80

Older studies have suggested an increased frequency of lower lobe TB as well as greater predisposition to cavitary lesion. This was reported more in the older patients. However studies by Parmer and Beyer have shown that lower lung field involvement is an infrequent location of pulmonary TB, occurring in 7% or less of patients with active pulmonary TB. Infiltrates are reported as predominant lesion in 22.58% by M.K. Jain et al 2003.

The average BMI of the patients in the study group was 22.74 in males and 22.08 in females. As BMI >25 was considered as exclusion criteria to eliminate a possible bias due to metabolic syndrome, naturally all the study patients will have BMI < 25, but the average was around 22 and there was no statistical correlation between IGT or DM and increased BMI. This can be explained by the fact that majority of patients attending our hospital belong to low socioeconomic status and the common factor of malnutrition and poor access to medical facilities may account for the above observation and also to the development of hitherto uncommon malnutrition related diabetes in both

IGT and normal group. Zack et al[49] (1973) Mugusi et al[75] (1990) also found no significant difference in BMI among the two groups.

Domicile

50.8% of study population belonged to urban domicile and 49.2% belonged to rural domicile in the present study.

	Urban	**Rural**
IGT	48%	13%
DM	24%	10%

IGT and DM was more among urban population. Statistically also the increased prevalence was significant $P< 0.05$. This process can be explained by overcrowding, life style modification and change in dietary habits promoting the conjoint presence of the brewing double trouble. This again reflects the conclusions of Ramachandran et al regarding prevalence of IGT and DM in urban population[19].

Tuberculosis occurring in the elderly age group has been claimed to be an important indicator of some underlying predisposing cause, the most important of which is diabetes. While diabetes in the elderly tuberculosis patients has received considerable attention in the past, the attention is now being focused more and more towards the younger age groups. It is being

realized that perhaps, the important pathogenic factor in the development of tuberculosis, even in the younger age group, could be a pre-diabetic state in some cases at-least. These instances, could lead to precipitation of frank diabetes. Such cases might be detected if properly investigated.

A significant group of young tuberculous patients may continue to remain in prediabetic state and some of these cases even though going into a phase of frank diabetes in the later stage may remain completely undetected.

The author tried to analyze the above mentioned fact and it is very well proved by the results of the study.

CONCLUSION

Prevalence of Impaired Glucose Tolerance in Tuberculous population of Madurai – was 31%, and it was significantly higher than in the general population.

Prevalence of Diabetes Mellitus in Tuberculous population of Madurai – 17% was also significantly higher than in the general population.

IGT was equally distributed in the study population regardless of age, whereas DM, was more in >35 age group.

The prevalence of coexisting diabetes mellitus and tuberculosis was more common among persons aged >35.

In the present study tuberculosis was found to be more among males.

Radiologically upper zone involvement was common in normal, IGT, as well as DM groups.

Infiltrate was the predominant lesion in all the three categories – normal, IGT and DM.

No significant gender difference was observed in glycaemic status of TB patients in this study.

SUGGESTIONS

It is worth remembering that early diagnosis of this combination of diabetes mellitus and tuberculosis is not that easy. When a combination of diabetes mellitus and tuberculosis is diagnosed either diabetes or pulmonary tuberculosis or both are already in the advanced stage and that makes management more difficult and thus the clinical outcome is rather poor.

From this study the following suggestions are made.

The only way to recognize this dreadful combination is to insist on

a. Routine blood sugar (fasting and post prandial) screening test in tuberculosis patients atleast for all persons above 35 years.
b. Follow up of patients with IGT – once a year for a future diabetes.
c. Chest X-ray has to be taken in a diabetic once a year as a routine
d. Sputum AFB, X-ray chest should be done in the following situations.
    i. more rapid weight loss
    ii. insulin requirement suddenly goes up
    iii. when cough persist for more than 3 weeks

SUMMARY

Tuberculosis is prevalent in developing countries where the incidence of diabetes is also increasing. The relationship among these two diseases is well known. As tuberculosis exerts stress, it is expected that susceptible pulmonary tuberculosis patients can develop diabetes mellitus. Keeping these concepts in mind, it was aimed to find out the prevalence of diabetes mellitus and IGT among pulmonary tuberculosis patients attending thoracic medicine unit of Government Rajaji Hospital, Madurai. Also it was planned to study their radiological aspects and finally to provide guidelines to detect one in another.

Thus 122 young sputum positive pulmonary tuberculosis patients attending out patient clinic of Thoracic Medicine Department of Government Rajaji Hospital, Madurai, who satisfied rigid inclusion and exclusion criteria were involved in this study and all the patients underwent oral glucose tolerance test.

32 of the 122 patients had IGT and 21 patients had diabetes mellitus. Thus the prevalence of IGT was 31.14% and diabetes mellitus was 17.21% among young sputum positive pulmonary tuberculosis patients. Males were predominantly affected by pulmonary tuberculosis almost twice as females, but the OGTT results didn't show any significant gender difference in glycaemic status.

IGT was equally distributed in the study population regardless of the age, but diabetes was more common in >35 age group, showing increased

prevalence of IGT among young Indian population. Regarding radiological finding, upper zone involvement was common p=0.0002 with infiltrates as predominant lesion (72.34%) in this study. Of the 122 patients 62 were of urban domicile and 60 were of rural domicile. Both, IGT and diabetes mellitus were significantly more in urban population with p value of 0.0005 and 0.0356 respectively.

BMI of the patients with IGT and diabetes mellitus didn't show any significant deviation from normal value probably because of the loss of weight produced by tuberculosis, also patients with BMI >25 were excluded from the study to rule out possible metabolic syndrome. Present observations show that there is a rising trend of IGT and diabetes mellitus among tuberculosis population when compared with previous study results from India and abroad. Possible mechanisms of coexistence of the two and the need for screening of these susceptible individuals were highlighted.

BIBLIOGRAPHY

1. Frenk J, Bobadilla JL, Sepulveda J, Lopez-Cervantes M: Health transition in middle-income countries: new challenges for health care. *Health Policy Plan* 4:29–39, 1989
2. Ramachandran, A., Snehalatha, C., Latha, E., Vijay, V. and Viswanathan,M., *Diabetologia*, 1997, **40**, 232–237.
3. Raman Kutty, Soman, C. R., Joseph, A., Pisharody, R. and Vijayakumar, K., *Natl. Med. J. India*, 2000, **13**, 287–292.
4. Misra, A., Pandey, R. M., Rama Devi, J., Sharma, R., Vikram, N. K. and Nidhi Khanna, *Int. J. Obesity*, 2001, **25**, 1–8.
5. Verma, N. P. S. and Madhu, S. V., *Diab. Res. Clin. Prac.*, 2000, **50**, 515, Suppl. 1.
6. Iyer, R., Upasani, S. and Baitule, M. N., *ibid*, 2000, **50**, 519, Suppl. 1.
7. Peter.H .Bennett and William.C.Knowler: Joslins diabetes mellitus Edn14, chap 19, 336-337, 2005,Lippincott Williams & Wilkins
8. Shafir. E. History & perspective of diabetes-Freund publishing house Ltd (1999)
9. Schadewalt.H.Diabetes ,its medical and cultural history.1987:43-100
10. Benedict SR.A modifaction of Lew Benedict method of estimating sugar in blood. Journal of biochemistry 1918;34:203-207

11. Lagusse E Structure et developpement du pancreas d` après les travaux recents. J Anat(Paris)1894;30:591-608
12. De Meyer.J. Archive Internationals de phisiologic1909:121-180
13. Bliss.M.The discovery of Insulin: University of Chicago press-1982
14. Nobel, The man and his prizes,Oklahoma:University of Oklahoma press 1951:221-223
15. King, H., Aubert, R. E. and Herman, W. H., *Diab. Care*, 1998, **21**,1414–1431
16. Ramachandran, A., Snehalatha, C., Anil Kapur, Vijay, V., Mohan, V., Das, A. K. and Rao, P. V., *ibid*, 2001, **44**, 1094–1101.
17. Ramaiya, K. L., Kodali, V. R. and Alberti, K. G. M. M., *Diab. Metabol. Rev*., 1990, **6**, 125–146.
18. Ramachandran, A., Snehalatha, C., Daisy Dharmaraj and Viswanathan, M., *Diab. Care*, 1992, **15**, 1348–1355
19. Ramachandran, A., Snehalatha, C., Latha, E., Manoharan, M. and Vijay, V., *Diab. Res. Clin. Prac.*, 1999, **44**, 207–213
20. Morse D, Brothwell D.R,Ucko P.J,.Tuberculosis in Ancient Egypt.Am Rev Respir Dis 1964;90:524
21. Koch R.Die Aetiologie der Tuberculose,A translation byBerna and max Pinner with an introduction by Allen.K.Krause Am Rev Tuberc1932;25:285

22. Maher D.Ravigilione.M.Global epidemiology of Tuberculosis. Clinics In Chest Medicine 2005;26:167-182
23. Breach J.H. Historical facts in diabetes mellitus Ann.Med.Hist.1928 10:387
24. Malins J Clinical diabetes mellitus.Eyre & Spottiswode, London,1968 P.268
25. Lalit kant, Diabetes Mellitus and Tuberculosis:The Brewing Double Trouble, Indian Journal Of Tuberculosis 2003;50 :4-183
26. King H, Aubert R.E, Herman WHO. Global burden of diabetes 1995-2025; Prevalence, numerical estimates, and projections.*Diabetes Care.*1998, 21, 1414
27. Ramachandran A, Snehalatha C, Viswanathan V. Burden of type-2 diabetes and its complications-the Indian scenario.*Current Science.* 2002; 83, 1471
28. Roy Chowdhary A.B.&Sen P.K.Diabetes inTuberculosis Patients.J Indian MA. Jan 1st1980.74;1:12
29. Mboussa J, Monabeka H, Kombo M, Yokolo D, Yoka-Mbio A, Yala F. Course of tuberculosis in diabetics. *Rev Pneumol Clin.*2003, 359, 39
30. Goswami R, Kochupillai N. Endocrine implications of tuberculosis. *In*: Sharma SK, Mohan A. (Eds). Tuberculosis. New Delhi: Jaypee Brothers Medical Publishers (P) Ltd, 2001, 386

31. Mark M.F.,Mosenthal H.O & Liu F: Diabetes Mellitus and Tuberculosis 1942 Am.J.M.Sc203:490
32. Reaud A:Diabetes and Tuberculosis1953 South M.J 46:248
33. Ferrara M.A. The Tuberculosis Diabetic Patient, 1952, New England J Med 246:55
34. Boucot K.R Diabetes Mellitus and Pulmonary Tuberculosis J Chronic Dis 1957:6:256
35. Jha G.N Singh V.S.Chourdia M.L.Chattopadhary S.K .Kumar S.R.& Agarwal K.S. Diabetes Mellitus with Pulmonary Tuberculosis, 1980 J.Diab .Asso.India Oc
36. Patel J.C. Desouza, Chervl, Jeghni SS Diabetes &Tuberculosis1977 Ind J Tub 24:155
37. Holden H.M & Hiltz J.E The Tuberculous Diabetes.1962.Canad Med Ass J 87:797
38. Nihalani K.D.Menon P, Perhar GS Mirchandani SM and Shanbhag VV Diabetes associated with Pulmonary Tuberculosis,1978 Hour Diab Ass. India:18:79
39. Goyal B.M.,Nigam. P,DubeyA.L Joshey L.D& Saxena H.N Study of Diabetes Mellitus in Pulmonary Tuberculosis 1978 J Diab Ass Ind 18:191

40. Deshmukh M.D. Master T.B.,David JC. and Tripathy. Diabetes complicated by Pulmonary Tuberculosis Diabetes in tropics p 49 edited by JC Patel & NG Tawalkar,1966:Dia. Ass. India. Bombay
41. Nanda C.N. Tripathy S.N. Association of Diabetes mellitus with Pulmonary Tuberculosis1968 JAPI:16;741
42. Fitz R. The Problem of Pulmonary Tuberculosis in patients with diabetes, 1930Am .J M.Sc180:192.
43. Boucot, K. R., Cooper, D. A., Dillon, E. S., Meljer, P. and Richardson, R., *Am. Rev. Tuberc.* 1952, 65 (Supplement Pp. 1-50), (The Philadelphia Survey
44. Basuglo DK, Bacakoglu F, Cok G, Sayiner A, Ates M. The Oral Glucose Tolerance Test in Patients with Respiratory Infections. Monaldi Arch for Chest Dis 1999; 54(4): 307-10.
45. Ezung T, Devi NT, Singh NT, Singh TB. Pulmonary tuberculosis and diabetes mellitus-a study. *J. of Indian MedicalAssociation.* 2002, 100, 376
46. Morris JT, Seaworth BJ, McAllister K. Pulmonary Tuberculosis in Diabetes. Chest 1992; 102 (2): 539-41.
47. Tsukaguchi K, Yonda T,Yoshikawa N ,Tokuyama T,Fu A,Tomassa K, Narita N,Enoki Y, Tsukaguchi M And Shrial F. Case study of interleukin -1 beta, tumour necrosis factor alpha and interleukin-6 production by

peripheral blood monocytes in patients with Diabetes Mellitus complicated by Pulmonary Tuberculosis. Kekkaku 1992;67:755-60

48. Bloom J.D. Glucose Intolerance in Pulmonary Tuberculosis. Am Rev Resp Dis 1969; 100: 38-41.
49. Zack M.B, Fulkerson LL, Stein E. Glucose Intolerance in Pulmonary Tuberculosis. Amer Rev Resp Dis 1973; 108: 1164-9. Study of Impaired Glucose Tolerance in Pulmonary Tuberculosis
50. Hadden DR. Glucose, Free Fatty Acids and Insulin Interrelations in Kwashiokar and Marasmus. Lancet 1967;2: 589-92
51. Guptan A, Shah A. Tuberculosis and Diabetes: An Appraisal. Ind J Tub 2000; 47(3): 3-8.
52. Roychoudhary AB, Sen PK. Diabetes in Tuberculosis Patients. JIMA 1980; 74: 8-13.
53. Mollentze WF, Pansegrouw D F, Steyn AF. Diabetes Mellitus, Pulmonary Tuberculosis and Chronic Calcific Pancreatitis Revisited. S Afr Med J 1990; 78 (5): 235-6.
54. Fernandez L, Hoskeri SN, Mesquita AM. Diabetes Mellitus in Pulmonary Tuberculosis. JAPI 1997; 45(10): 774-76.
55. Swai ABM, Alberti KGMM, Mclarty DG. Increased Prevalence of Diabetes Mellitus in Patients with Pulmonary Tuberculosis in Tanzania. Tubercle 1990; 71: 271-6.

56. Nichols, G.P., Am. Rev. Tuberc. 1957, 76,1016Banyai, A. L., *Am. Rev. Tuberc.* 1931,24, 50

57. Shaikh MA. Singla R, Khan NB, Sharif NS, Saigh MO. Chest 1994 Jul 106 (1) : 326.

58. D.C. Lahiri and P.K. Sen (From B.C. Roy Research Institute, Calcutta). Indian J. Tub.Vol. X, XI, No.2, 1974

59. P.A. Desh Mukh and T.Shaw Ind. J. Tub. 1984, 31, 114.

60. S.R. Tripathy et al Ind. J. Tub. 1984, 31, 122.

61. Research committee of tuberculosis association of India. Ind. J. Tub. 1987, 34, 91.

62. DM – TB – The brewing double trouble by Lalit Kant**.** Ind. J. Tub. Vol 50No.4, Oct. 2003.

63. Banyai, A. L., *Am. Rev. Tuberc.* 1931,24, 50.

64. Wiener, J.J. and Kavee, J. Am. Rev. Tuber. 1936, 34, 179.

65. Rest , A., Am. Rev. Tuberc,. 1941, 43, 314

66. Israel, H. L., and Payne, H. M., *Am. Rev. Tuberc. 1940, 41, 188.*

67. Banyai, A. L., and Cadden, A. V., *Arch. Inl*3.).

68. Speck, C.D. J. R. Dross, R.L. and Mendell,H.E., New Orleans M. & S. J. 1952, 04,493.

69. Ferrara, M.A., *New England .J. Med.* 1952, 246’ 55’ . . Nichols, G.P., Am. Rev. Tuberc. 1957, 76,1016.

70. Reaud, A., South M. J., 1953, 46, 248

71. Khanna BK. Pulmonary Tuberculosis Diabetes Mellitus. JIMA 1968; 50(9): 407.

72. Kishore B, Nagrath SP, Mathur KS, Hazra DK, Agrawal BD. Manifest, Chemical and Latent Diabetes in Pulmonary Tuberculosis. JAPI 1973; 21: 875-881.

73. Marais R.M. Diabetes Mellitus in Black and Colored Tuberculosis Patients. S Afr Med J 1980; 57: 483-4.

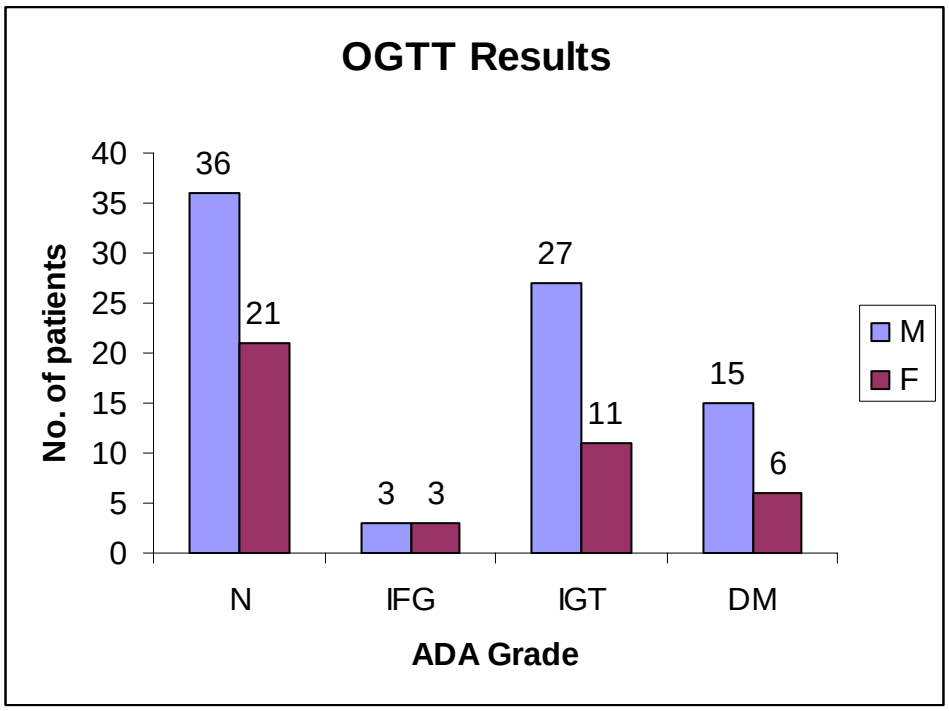
74. Gulbas Z, Erdogan Y, Balci S. Impaired Glucose Tolerance in Pulmonary Tuberculosis. Eur J Respir Dis 1987; 71(5): 345-7.

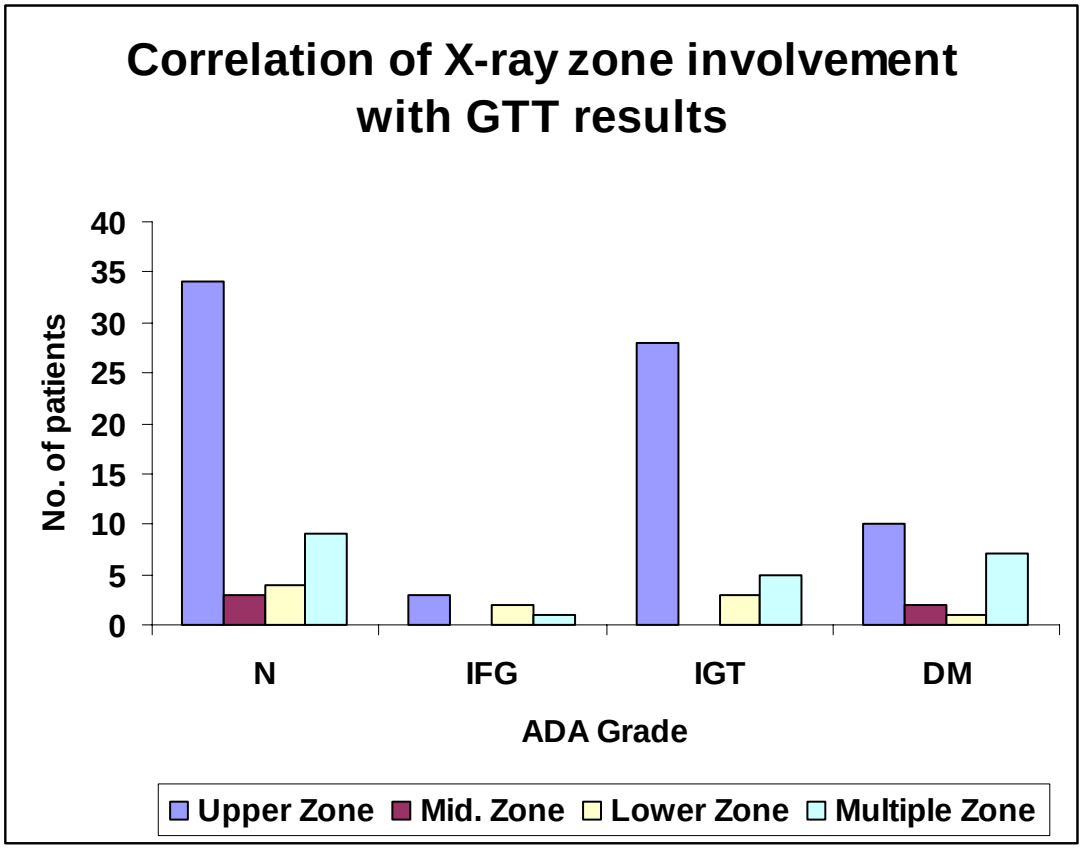
75. Mugusi F, Swai ABM, Alberti KGMM, Mclarty DG. Increased Prevalence of Diabetes Mellitus in Patients with Pulmonary Tuberculosis in Tanzania. Tubercle 1990; 71: 271-6.

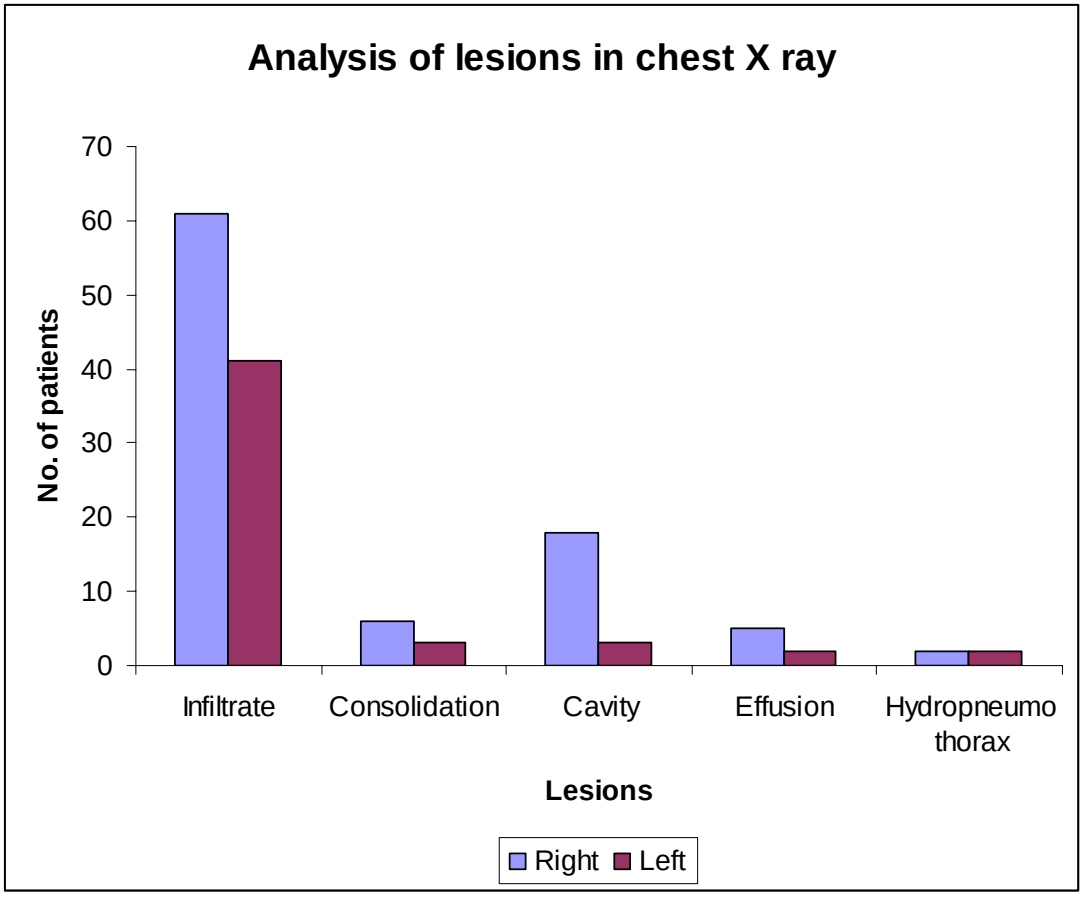
76. Jawad F, Shera AS, Memon R, Ansari G. Glucose Intolerance in Pulmonary Tuberculosis. J Pak Med Asso 1995; 45(9): 237-8. 3 Khanna BK. Pulmonary Tuberculosis Diabetes Mellitus. JIMA 1968; 50(9): 407-12.

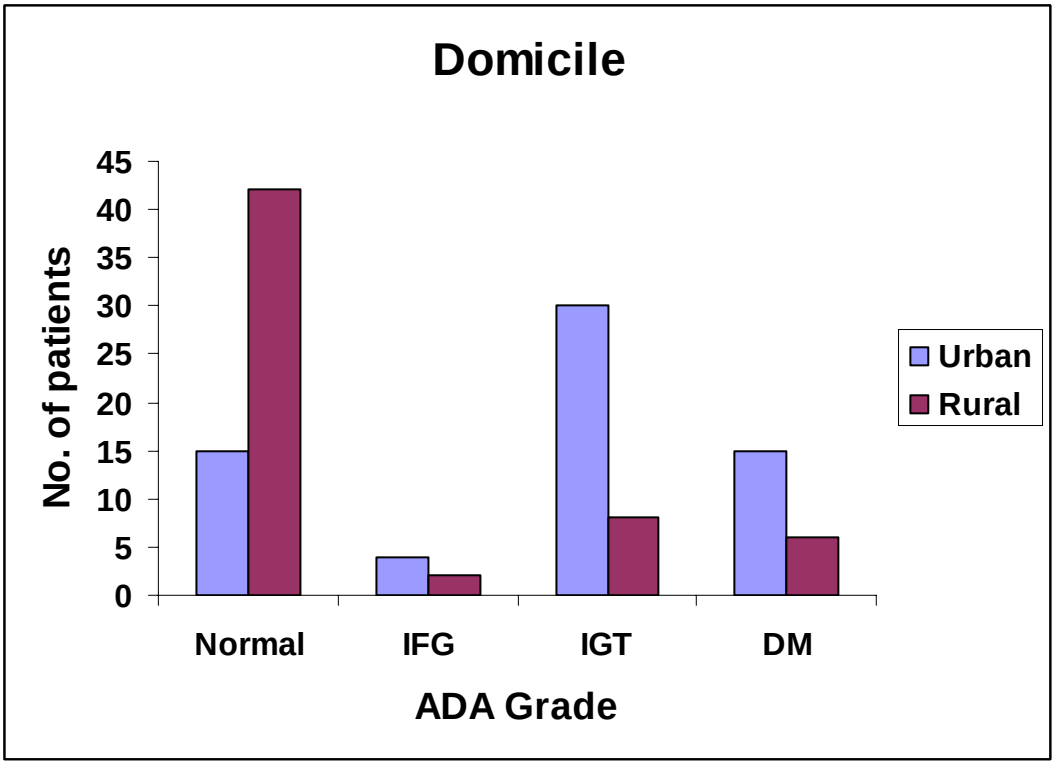
77. Lin S, Shen M, Sun Y. Epidemiological Characteristics of Tuberculosis Patients Complicated with Diabetes in Shanghai. Zonghua Jie He He Hu Xi Za Zhi 1998; 21(8): 504-6.

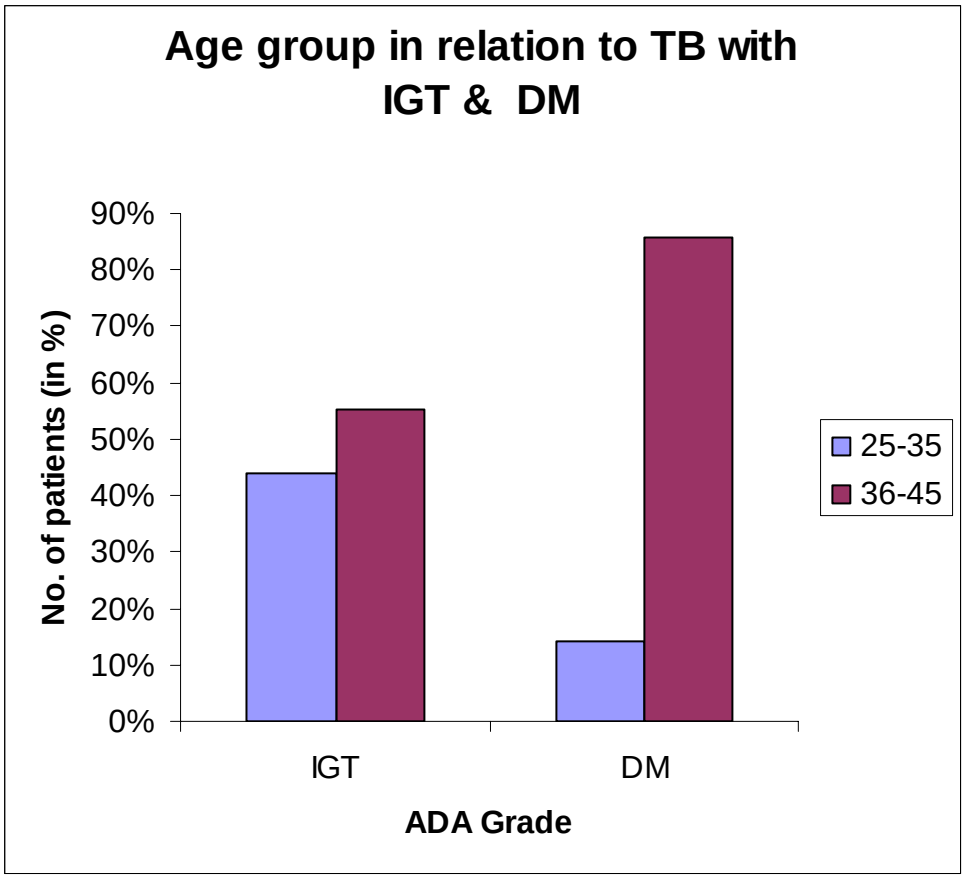
78. Chukanova V.P, Sergeev A.S, Pospelov L.E, Sobkin A.L. Epidemiological and lmmunogenetic Analysis of Tuberculosis and Diabetes Mellitus Association. Probl. Tuberk 2000; (4): 11-14.
79. Yamagishi F, Sasaki Y, Yagi T, Yamatani H, Kuroda F, Shoda H. Frequency of Complication or Diabetes Mellitus in Pulmonary Tuberculosis. Kekkaku 2000; 75(6): 435-7
80. Firsova VA, Ovsiankina ES, Kaminskaia GO, Rura Koval, Grigoreva ZP. Carbohydrate Metabolism Impairment and Specific Features of the Course of Tuberculosis in Adolescents with Diabetes Mellitus. Problemy Tuberkuleza 2000; 4: 17-19
81. M.K Jain, PK Baghel, R Agarwal, Study of ImpairedGlucose Tolerance in Pulmonary Tuberculosis Patients.Indian Journal Of Commmunity Medicine2006 ,31;3:137-139
82. Gajanan Gavde, clinical Review. The lung in Diabetes Mellitus, Lung India, 1994,12(2),94


OGTT Results
No. of patients
40
35
30
25
20
15
10
5
0
36
21
3
3
27
11
15
6
N
IFG
IGT
DM
ADA Grade
M
F

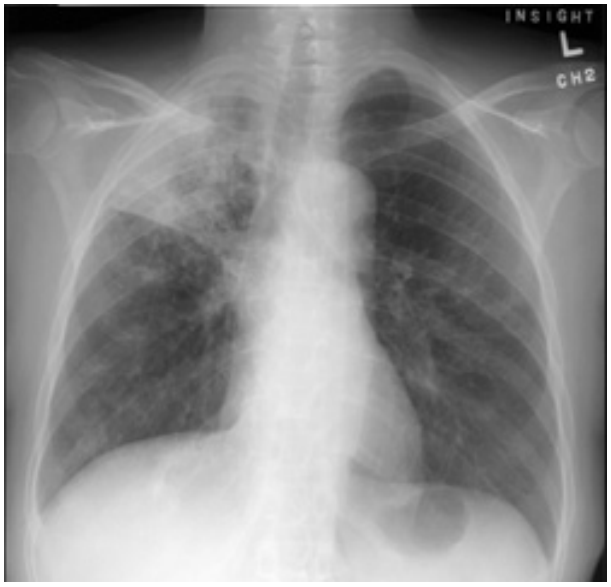

Correlation of X-ray zone involvement with GTT results
No. of patients
40
35
30
25
20
15
10
5
0
N
IFG
IGT
DM
ADA Grade
Upper Zone
Mid. Zone
Lower Zone
Multiple Zone


Analysis of lesions in chest X ray
70
60
50
40
30
20
10
0
No. of patients
Infiltrate
Consolidation
Cavity
Effusion
Hydropneumo thorax
Lesions
Right
Left


Domicile
No. of patients
45
40
35
30
25
20
15
10
5
0
Normal
IFG
IGT
DM
ADA Grade
Urban
Rural


Age group in relation to TB with IGT & DM
90%
80%
70%
60%
50%
40%
30%
20%
10%
0%
No. of patients (in %)
IGT
DM
ADA Grade
25-35
36-45

CHEST X-RAY IN A PATIENT WITH IGT



CHEST X-RAY IN A PATIENT WITH DM

APPENDIX - II

PROFORMA

A STUDY ON GLUCOSE TOLERANCE TEST IN YOUNG SPUTUM POSITIVE TUBERCULOSIS PATIENTS

Personal Data :

Name :

Age :

Sex :

Address :

Income :

Family History :

a. TB
b. DM

Other comorbid conditions

BMI :

Sputum AFB :

Chest X-ray :

GTT: Blood Glucose

Fasting

1 hr PP

2 hr PP

APPENDIX III

MASTER CHART KEY

1. Sex M – Male F – Female

2. GTT result BSF – Blood Sugar Fasting

1 hr PP – 1 hour post prandial

2 hr PP – 2 hour post prandial

3. ADAGr. – American Diabetology Association Grade

4. X – ray

Side R – Right L – Left

Zone 1- Upper zone 2 – Mid zone 3 – Lower zone

Lesion Infilt – Infiltrates Con – Consolidation

Eff. – Effusion Hydrop – hydropneumothorax

5. BMI – Body Mass Index

CONTENTS

APPENDIX -I

Ethical Clearance

K. Dis.No. 7076/E4/1/2006

Govt. Rajaji Hospital,
Madurai – 625 020. Dt. 05.05.2006.

Sub: Establishment – Govt. Rajaji Hospital, Madurai – Ethical Committee
Projects approved by the Committee – Intimation – Sent – Reg.

The Ethical Committee of the Govt. Rajaji Hospital, Madurai was held at 12 Noon on 27.04.2006 at the Dean's Chamber, Govt. Rajaji Hospital, Madurai, and the following Projects were approved unanimously by the Committee Members.

S.No.	Name of the Student	Name of the Project approved
01)	Dr.S.Jawahar, PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Co-relation of CRP levels in CRF patients with Cardiovascular complications.
02)	Dr.J.Sarva Vinothini, PG in MD(Anaes.) Madurai Medical College,Mdu.	Status of Cancer pain – an epidemiological Survey.
03)	Dr. S.Senthur Rajapandian, PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Serum Uric acid level in Type II Diabetes Mellitus.
04)	Dr.T. Muthuvel, PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Pulmonary function test in Chronic male Smokers.
05)	Dr.P. Sankar PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Prevalence of Intestinal parasites in HIV patients
06)	Dr. M. Senthil Babu PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Serum Ferritin level in congenital Cyanotic Heart disease.
07)	Dr.V. Anand, PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Serum Calcium level in newly Diagnosed Hypertension.
08)	Dr.S. Sivakumar PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Clinical profile of "Lean body weight" Type 2 Diabetes Mellitus Patients in comparison with Obis and normal weight – Type II D.M.patients.
09)	Dr. S. Ramesh PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Analysis of LIPID Profile abnormalities among Post renal transplant patients.
10)	Dr. S. Srikumar, PG in MD(Gen.Med.) Madurai Medical College,Mdu.	A Study of Ischaemic Mitral Regurgitation.
11)	Dr. R.V. Sebasan PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Study of Intra cavitary thrombus in Thrombolytic Era.
12)	Dr.C. Ananthi. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Hepato biliary abnormalities in HIV Suspositive patients.
13)	Dr.N. Periasamy. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Pulmonary function test in Rheumatic Mitral Stenosis.
14)	Dr. Usha Nagadevi.C.S. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	GTT in young sputum positive pulmonary Tuberculosis patients.
15)	Dr.S. Gokulnath. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Clinical analysis of Wilson disease & Clinical studies in Acute Leukaemia
16)	Dr.R. Omnath PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Coorelation between Cardiac isoform of Alfa 2 – Macroglobulin and cardiac involvement in HIV/AIDS patients.

17)	Dr.S. Palanisamy PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Echocardiographic assessment of Cardiac dysfunction in patients of Type II Diabetes Mellitus without Cardiac symptoms.
19)	Dr.J. Thirumalirajan. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Risk profiles in Cerebro-vascular Accidents.
20)	Dr.B.J. Gokul PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Prevalnce of Urinary tract infection in patients with ST elevation Myocardial infarction.
21)	Dr.V.M. Manikandan PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Coorelation between HIV and Cardiac diseases in patient around Madurai- Molecular analysis.
22)	Dr.M. Johnsi rani. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Anthropometric measurements among Type II Diabetes Mellitus patients.
23)	Dr.V.L. Alaga Venkatesan. PG in MD(Gen.Med.) Madurai Medical College,Mdu.	Clinical and Radiological presentation of Adults with Smear Positive Tuberculosis in Govt. Rajaji Hospital,Madurai.

Please note that the investigator should adhere the following:-

11) She/He should get a detailed informed consent from the patients/participants and maintain confidentially.
12) She/He should carry out the work without detrimental to regular activities as well as without extra expenditure to the Institution or Government.
13) She/He should inform the Institution Ethical Committee in case of any change of study procedure site and investigation or guide.
14) She/He should not deviate for the area of the work for which applied for Ethical clearance.
15) She/He should inform the IEC immediately, in case of any adverse events or serious adverse reactions.
16) She/He should abide to the rules and regulations of the Institution.
17) She/He should complete the work within the specific period and apply for, if any extension of time is required, She/He should apply for permission again and do the work.
18) She/He should submit the summary of the work to the Ethical Committee on completion of the work.
19) She/He should not claim any funds from the Institution while doing the work or on completion.
20) She/He should understand that the members of IEC have the right to monitor the work with prior intimation.

Dean i/c / Chairman,
Ethical Committee, Govt. Rajaji Hospital, Madurai.

APPENDIX III
MASTER CHART

Sl.NO	AGE	SEX	B.S.F	1HrPP	2HrPP	ADA Gr.	SPUTUM A	SPUTUM B	SPUTUM C	ZONER	ZONEL	LESIONR	LESIONL	BMI
1	34	M	89	146	160	IGT	1+	1+	1+	1		INFIL		20
2	32	M	82	126	146	IFG/IGT	1+	1+	1+	1		INFIL		24
3	33	M	72	134	166	IGT	1+	1+	1+	1		INFIL		23
4	44	M	148	168	200	DM	3+	2+	1+		1	INFIL		20
5	40	F	70	100	120	N	1+	1+	2+			EFF		22
6	38	M	72	105	126	N	_ve	1+	1+	1	2	INFIL	INFIL	28
7	42	F	111	133	125	IFG	1+	1+	_ve	3	3	INFIL	INFIL	24
8	40	F	107	180	193	IGT	2+	2+	1+	1	1	CAVITY	INFIL	23
9	33	M	69	151	140	IGT	1+	1+	1+			EFF		21
10	44	M	148	168	200	DM	3+	2+	2+				HYDROP	22
11	30	F	68	120	120	N	_ve	1+	1+	1		CAVITY		25
12	45	F	140	280	312	DM	3+	1+	2+	1	2&3	CAVITY	INFIL	23
13	42	M	62	122	138	N	_ve	1+	1+	1		INFIL		23
14	29	M	76	106	123	N	1+	1+	_ve		1		CON	24
15	40	M	78	128	148	IGT	1+	1+	1+	1		INFIL		21
16	26	M	75	121	130	N	1+	1+	1+	1&3		INFIL		21
17	30	F	100	148	168	IGT	2+	3+	3+	3		INFIL		22
18	38	F	92	197	140	IGT	1+	1+	1+		1	INFIL		23
19	39	M	109	132	126	N	1+	1+	1+	1		INFIL		22
20	42	M	72	138	166	IGT	_ve	1+	1+		123	INFIL		24
21	40	M	80	106	120	N	scanty-6	scanty4	scanty7	1		INFIL		24
22	37	M	68	120	130	N	1+	1+	1+		123	INFIL		23
23	43	M	999	155	189	IGT	1+	_ve	1+	1	123	INFIL	INFIL	22
24	38	F	111	138	125	N	1+	1+	1+	2	23	CAVITY	INFIL	24
25	38	F	60	80	96	N	_ve	scanty-6	1+		1		INFIL	23
26	43	M	85	105	134	N	1+	1+	1+		1		INFIL	20
27	25	F	86	132	105	N	1+	scanty7	scanty8		1		INFIL	21
28	45	M	145	168	203	DM	_ve	1+	1+	2		CAVITY		29
29	25	F	88	123	134	N	_ve	1+	1+	1	1	INFIL	INFIL	23
30	27	F	75	108	91	N	1+	3+	3+	1		INFIL		22
31	26	M	73	174	167	IGT	1+	1+	1+		1		INFIL	24
32	27	M	120	132	136	IFG	1+	_ve	_ve		1	CAVITY		23
33	40	M	77	98	80	N	1+	1+	1+	1		CAVITY		22
34	29	M	90	144	156	IGT	1+	1+	1+		1		CAVITY	21
35	42	F	62	112	77	N	_ve	1+	1+	1		INFIL		22
36	44	M	90	173	196	IGT	3+	3+	3+	3		HYDROP		22
37	37	M	79	111	130	N	_ve	1+	1+	1		INFIL		22
38	26	M	89	146	158	IGT	2+	2+	2+	123	123	INFIL	INFIL	23
39	25	M	78	123	128	N	2+	2+	1+	13	123	CAVITY		21
40	45	M	111	284	264	DM	1+	3+	3+		1		INFIL	27
41	40	M	90	123	134	N	1+	1+	scanty9	1		CON		22
42	45	M	88	189	203	DM	3+	3+	3+	123	123	INFIL	INFIL	26
43	25	F	87	119	109	N	1+	1+	1+	1	1	INFIL	INFIL	21

Sl.NO	AGE	SEX	B.S.F	1HrPP	2HrPP	ADA Gr.	SPUTUM A	SPUTUM B	SPUTUM C	ZONER	ZONEL	LESIONR	LESIONL	BMI
44	25	F	70	135	169	IGT	_ve	1+	1+		12		INFIL	22
45	43	M	79	110	134	N	_ve	2+	1+	1		INFIL		23
46	35	M	74	114	108	N	1+	1+	1+		1		INFIL	21
47	44	M	88	151	177	IGT	1+	1+	1+	1		CAVITY		20
48	25	F	78	120	123	N	_ve	1+	1+	2		CAVITY		23
49	45	M	78	177	202	DM	1+	2+	2+	1		INFIL		26
50	45	M	87	112	134	N	1+	1+	1+	1		CAVITY		21
51	34	M	134	206	234	DM	3+	3+	3+	1		INFIL		28
52	43	M	90	195	201	DM	1+	1+	1+	123	123	INFIL	INFIL	25
53	43	M	114	165	188	IGT	1+	1+	1+	1		INFIL		22
54	27	F	404	304	216	DM	1+	1+	1+	1		INFIL		22
55	45	M	89	125	134	N	1+	1+	1+		1	INFIL		23
56	45	F	98	183	206	DM	_ve	2+	1+		2	CAVITY		26
57	45	M	87	145	165	IGT	3+	3+	2+	1		INFIL		24
58	26	F	75	154	144	N	1+	1+	1+	13		INFIL		21
59	45	M	168	261	263	DM	1+	1+	2+		1		INFIL	23
60	28	M	164	201	388	DM	2+	2+	2+		1		INFIL	21
61	29	M	79	185	168	IGT	2+	2+	2+	1	1	INFIL	INFIL	21
62	32	M	88	156	188	IGT	3+	1+	1+	1		INFIL		24
63	43	M	69	125	135	N	_ve	1+	1+	3		CON		21
64	35	F	86	114	124	N	1+	1+	1+			EFF	EFF	23
65	39	F	82	123	114	N	1+	1+	1+	1		CAVITY		23
66	40	M	96	156	187	IGT	1+	1+	1+		1		INFIL	21
67	43	M	125	114	120	IFG	1+	1+	1+		1		INFIL	20
68	41	F	99	135	124	N	_ve	1+	1+	1		INFIL		22
69	26	F	104	125	134	N	1+	1+	_ve	1		INFIL		23
70	42	M	94	156	192	IGT	1+	1+	1+	1		INFIL		21
71	44	M	84	115	127	N	1+	2+	1+		1		INFIL	21
72	28	F	114	128	136	IFG	1+	1+	1+	12		INFIL		20
73	36	M	89	136	166	IGT	1+	1+	2+		3	CON		22
74	44	F	86	125	132	N	1+	2+	1+	1		INFIL		24
75	41	M	98	125	133	N	1+	1+	1+	1		INFIL		23
76	39	M	74	145	169	IGT	1+	1+	1+		1		INFIL	21
77	33	F	86	124	132	N	1+	1+	1+		1		INFIL	22
78	35	M	89	125	136	N	1+	1+	2+	1		CAVITY		21
79	42	M	102	145	186	IGT	1+	1+	1+	1		INFIL		23
80	44	M	115	186	225	DM	3+	2+	2+	1		INFIL		26
81	28	F	98	128	126	N	1+	1+	1+		1		INFIL	21
82	33	F	88	154	168	IGT	1+	1+	1+	1		INFIL		22
83	35	F	99	156	178	IGT	1+	1+	1+	1		INFIL		23
84	39	M	114	168	229	DM	3+	3+	2+		1		INFIL	25
85	41	M	96	114	125	N	1+	1+	1+	1		CAVITY		22
86	40	M	129	179	231	DM	2+	1+	2+		1		CAVITY	27
87	43	M	74	106	114	N	_ve	1+	1+		1		INFIL	22
88	26	F	124	135	126	N	_ve	1+	1+	1		INFIL		20
89	29	M	77	128	134	N	1+	1+	1+	12		INFIL		23
90	30	M	100	149	171	IGT	2+	2+	1+		1		INFIL	23

Sl.NO	AGE	SEX	B.S.F	1HrPP	2HrPP	ADA Gr.	SPUTUM A	SPUTUM B	SPUTUM C	ZONER	ZONEL	LESIONR	LESIONL	BMI
91	25	M	84	124	132	N	1+	1+	1+			CON		22
92	35	M	96	125	135	N	1+	1+	1+	1		INFIL		21
93	33	F	96	147	168	IGT	1+	1+	1+	1		INFIL		24
94	27	M	84	125	136	N	1+	1+	1+		1		CAVITY	22
95	37	M	92	105	124	N	1+	1+	ve		1		INFIL	21
96	32	F	93	135	167	IGT	3+	1+	1+	1		INFIL		22
97	41	M	125	169	245	DM	2+	2+	1+	12		INFIL		25
98	35	F	96	112	125	N	1+	1+	1+	3		CON		22
99	45	F	128	184	268	DM	2+	2+	1+		1		INFIL	25
100	25	M	78	115	137	N	1+	1+	1+		3		CON	23
101	26	F	84	114	125	N	1+	1+	1+	1		INFIL		21
102	31	M	112	126	135	IFG	1+	1+	1+		1		INFIL	22
103	30	M	95	125	135	N	1+	1+	1+	123		INFIL		21
104	26	M	86	124	134	N	1+	1+	1+	1	1	INFIL	INFIL	23
105	42	M	112	158	163	IGT	3+	1+	2+	1	1	CAVITY	INFIL	25
106	44	F	96	154	178	IGT	1+	1+	1+	1	1	INFIL	INFIL	23
107	41	F	112	158	225	DM	2+	2+	1+	3		CON		25
108	43	M	95	158	194	IGT	3+	1+	1+			EFF	EFF	25
109	29	M	88	102	124	N	1+	1+	1+	1		INFIL		21
110	35	M	76	131	135	N	1+	1+	1+	12		INFIL		21
111	39	F	95	145	168	IGT	1+	2+	1+		1		INFIL	24
112	38	M	91	125	146	IGT	1+	1+	1+			EFF		24
113	26	M	88	124	135	N	1+	1+	1+		3		CON	21
114	29	F	124	135	126	IFG	1+	1+	1+			HYDROP		23
115	35	M	95	125	134	N	1+	1+	1+		1		INFIL	22
116	42	M	121	158	177	IGT	1+	1+	2+	1	1	INFIL	INFIL	24
117	44	F	152	198	257	DM	3+	1+	1+	1		CAVITY		26
118	38	M	89	124	134	N	1+	1+	1+	1		CAVITY		22
119	35	F	95	145	175	IGT	2+	2+	1+	1		INFIL		25
120	27	M	88	121	136	N	1+	1+	1+	1	1	INFIL	INFIL	21
121	43	M	124	165	239	DM	1+	1+	1+	12		INFIL		24
122	42	M	94	135	168	IGT	2+	1+	2+	1	1	INFIL	INFIL	24

DOMICILE
Urban
Urban
Urban
Urban
Rural
Urban
Urban
Urban
Urban
Urban
Rural
Urban
Rural
Urban
Rural
Rural
Urban
Urban
Urban
Urban
Urban
Rural
Urban
Rural
Rural
Rural
Urban
Urban
Urban
Urban
Rural
Rural
Rural
Urban
Urban
Rural
Urban
Urban
Urban

DOMICILE
Urban
Urban
Urban
Urban
Urban
Urban
Rural
Urban
Urban
Urban
Rural
Rural
Urban
Urban
Rural
Rural
Urban
Urban
Urban
Rural
Rural
Rural
Rural
Rural
Rural
Rural
Urban
Rural
Urban
Rural
Rural
Rural
Urban
Rural
Rural
Urban
Urban
Rural
Rural
Urban
Rural
Rural
Rural
Rural
Urban

DOMICILE
Rural
Rural
Urban
Rural
Rural
Urban
Urban
Urban
Urban
Rural
Rural
Rural
Rural
Rural
Rural
Urban
Rural
Urban
Urban
Rural
Urban
Rural
Rural
Urban
Urban
Urban
Urban
Rural
Urban
Rural
Urban
Rural